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VOLUME XIV NUMBER 2

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STUDIES FROM THE Department of PEDIATRICS

1922/24

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477 FIRST AVENUE
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young infants this stage of tuberculosis is practically always a general miliary tuberculosis. Very rarely there are isolated lesions in bones and joints, in the viscera or serous membranes. The older the infant or child the more likely is the tertiary lesion to be localized instead of general, leading to involvement which is more easily recognized and of more favorable prognosis.

For practical consideration the portals of entry in infantile tuberculosis are ordinarily two, either pulmonary or enteric. The rarer modes of entry, such as through the tonsils or skin, are usually readily recognized and consideration of these is beyond the scope of this paper. In the pulmonary form of the disease it would seem at the present time that the conception of Ghon is the most acceptable and best in accord with the available evidence. On entry, the tubercle bacilli cause a small local pulmonary lesion which heals very rapidly and causes no symptoms whatever. From this primary lesion, however, arises an infection of the mediastinal lymph nodes and it is here that the fate of the organism is decided. The disease may heal in rare instances. It may lie latent for a long period of time. It may spread very rapidly and give rise to general tuberculosis or to a localized lesion. In the enteric form of infection which is due probably in most instances to the bovine bacillus, we do not know at the present time the nature of the primary lesion, or whether a definite one comparable to the pulmonary lesion of Ghon occurs at all. We do not know whether there occurs in the mucous membrane of the intestine a local lesion or whether the tubercle bacilli may pass through the intestinal wall without producing a local

lesion. There have been a considerable number of observations on this subject, but it is at present quite undecided. It is sufficient for our purpose to know that there occurs a secondary lesion in the mesenteric lymph nodes and here the focal disease follows the same course as it may pursue in the mediastinal glands.

No consideration of tuberculosis can evade the important question of prevention and before discussing diagnosis I shall have a few words to say on this subject. Preventive measures which are widespread and due to the activity of many agencies have done much to limit the infection of young individuals. The ideal, of course, would be absolute prevention, but until we are able to recognize tuberculosis in the adult earlier this result will probably not be obtained. It is therefore probable that for many years to come we shall be confronted with tuberculosis in young infants.

About the enteric form of infection I think there is a little to be said. In many instances it is due to the bovine bacillus and is usually a milk-born infection. In the greater number of larger cities today all the milk for general consumption must be either pasteurized or certified. Milk properly pasteurized is, of course, free from living tubercle bacilli. I question whether the same can be said of certified milk at the present time. I think most of us are in the habit of boiling all milk for infant feeding. This is done partly for reasons other than the prevention of tuberculosis. The lack of protection from certified milk may arise from two sources. An animal very recently infected with tuberculosis may be admitted into a herd at which time the test is negative. In such instances it is possible for the disease to

involve the udder and to be transmitted to other animals before the next tuberculin test reveals the infection. A second cause of danger is the fact that the reactivity to tuberculin of an infected animal can be suppressed by giving a large dose of tuberculin. This renders it possible for dishonest dealers successfully to dispose of infected cows as tuberculosis-free. How great is the danger from certified milk cannot be stated. Certainly it is small, but it is equally certain that to some degree the danger is real as is attested by actual experience. It therefore seems to me that the whole problem must resolve itself into the answer of the comparatively simple question whether the good that can arise from the feeding of raw certified milk is greater than the danger of the transmission of infection with the bovine tubercle bacillus in this way. Bovine tuberculosis is certainly a factor to be reckoned with, as it probably comprises, at least in a number of cities in this country, from 12 to 25 per cent of the tuberculous infections in early life.

In regard to symptomatology it is perfectly obvious that if we are to do anything in controlling the large mortality of tuberculosis in infants the disease must be recognized in its secondary or glandular stage. It is rather interesting that the diagnosis of tuberculosis in infancy is made more often in hospital patients than in private patients and the reason is obviously that all patients entering the hospital are subjected to a very careful study, including a routine tuberculin test. I have been interested in going over the histories of infants with tuberculosis in which the families were sufficiently intelligent to give very careful and reliable histories and in practically all of these cases there

was a period in the infant's life during which there were present definite symptoms almost unquestionably due to the secondary or glandular stage of tuberculosis. These symptoms were often very mild. They were not definite and could have been due to other causes, but they were present in nearly all cases. The most prominent was the history of a period during which the infant who had previously thrived did not do so well. There was failure to gain and there was definite pallor. In practically all there was a history of a low grade of fever and oftentimes a rise to 101 degrees or more. In cases of the pulmonary form there was in most cases a history of cough. The cough, as a rule, was infrequent and mild, but it was persistent. In a few cases of enteric infection there were similar symptoms. The general symptoms were practically identical with those present in the pulmonary form with the exception of cough. In both groups of cases there was at times a tendency to vomiting and diarrhea. Such symptoms may last only a short period of time, a few weeks, a month or two, and may then disappear. The symptoms due to the infection may continue and gradually merge into symptoms of tuberculous meningitis or acute general miliary tuberculosis. As all of you know, there is rarely the development of an extreme degree of emaciation such as is commonly supposed to accompany tuberculosis. I am sure we have all been struck at numerous times by the fact and have remarked upon it that an infant may come into the hospital with tuberculous meningitis or general miliary tuberculosis with slight if any impairment of its nutrition. In other words, we have to deal in infants with a secondary or glandular state of tu-

berculosis which causes very few symptoms, which does not make the infant particularly ill, from which general tuberculosis develops very rapidly. In the recognition of the secondary stage the physical signs are unfortunately of little use. It is only in cases where there is a tremendous enlargement of the mediastinal or mesenteric lymph nodes that we get definite physical signs. I will not enter upon a discussion of the usefulness of D'Espine's sign because in small infants it is very difficult to elicit and in my experience is of little value unless the granular enlargement is of great degree. Greatly enlarged mesenteric lymph nodes may be palpated in some cases, leading to a presumptive diagnosis which may be confirmed by a tuberculin test. There are only two objective means at our disposal which should enable us to make a definite diagnosis in the pulmonary form. One is the use of the tuberculin test and the other is the information given by the x-ray. In regard to the tuberculin test I think we have all come to appreciate the fact that the cutaneous test alone is not sufficient and that in suspicious cases one should resort to the intracutaneous test, using at least 0.2 milligrams of tuberculin before one can consider the test negative. By these two means most of the cases can be recognized, for in the young individual a positive tuberculin test is always of significance.

Up to the last few years a positive tuberculin test alone in young infants was considered of practically fatal prognostic import. It was generally felt that the resistance of young infants to tuberculous infections was low and that once infected a catastrophe would almost invariably occur. That this is true in many instances

there can be no question. For some years I was connected with an institution which dealt with a great number of supposedly well infants. These infants on admission to the institution homes were all tested with tuberculin. A large number of those with positive cutaneous tests succumbed to tuberculous meningitis or general miliary tuberculosis within a year or so. The results, however, among the better classes where appropriate treatment can be given are very different. I have been in contact with, or have knowledge of a number of cases in private practice where the disease was recognized early and the parents were in position to give the infants appropriate treatment. In these cases there were only two fatalities, which is in marked contrast to the usual experience, and I think furnishes sufficient evidence that tuberculosis in infancy recognized at the proper time is far from being an entirely hopeless condition. Indeed, it is my belief that if recognized early in the secondary stage when the infant is in a fair condition of nutrition, the prognosis is not extremely grave provided proper care and treatment are available.

In regard to the treatment there is very little to say. It is essentially the same as for other forms of tuberculosis. The infant is kept out of doors constantly. The food is carefully regulated, giving proper amounts, avoiding overfeeding and particularly overfeeding with fat, and making every effort to avoid digestive symptoms. The use of heliotherapy is of the greatest value. In addition to direct sunlight the ultraviolet light is of use in supplementing treatment with the sun's rays. It is used on the days when the sun does

not shine. In the use of both the object should be to produce a very marked tanning of the skin. Of the greatest importance is the prevention of infections, especially measles, whooping cough and common colds. To insure this protection the infant should be carefully isolated from all sources of infection, either actual or potential.

In conclusion, I wish to summarize very briefly the important feature of tuberculosis in young infants. Most if not all infants succumbing to generalized tuberculosis have passed through a stage during which the disease was localized and latent and if the disease had been recognized at that time the chances for effective treatment would have been good.

MISTAKEN DIAGNOSES IN INFANTS AND CHILDREN *

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The opportunity to check clinical diagnoses with necropsy findings is available to all hospitals with an active pathologic service. Reports, however, are infrequent, and the analysis here presented, from the New York Nursery and Child's Hospital, covering a period of three years, is presented with the hope that it will lead to similar studies.

Cabot's [1] contribution is well known, and any one intending to pursue such studies will do well to heed his admonitions. He says in part:

> It is not a simple matter to collate antemortem and postmortem data in an intelligent way. One cannot simply read off the clinical diagnoses and note their correspondence or lack of it with the anatomic findings, for:
>
> 1. It is often obvious when one reads the clinical record that the diagnosis has been copied from the autopsy protocol.
>
> 2. The clinical diagnosis may be so abbreviated as to omit important facts known during life. . . .
>
> 3. In some cases it has been clear, after a little study, that the clinical diagnosis actually written in the records had been hurriedly filled in by an intern and did not represent the opinion of the attending physician. . . .
>
> My comparisons, then, have been far from literal. In each case I have gone behind the recorded diagnoses and endeavored to reason out what diagnosis was justified by the facts as known during life.

All of the foregoing wise counsel applies equally well to the pediatrician in his studies with infants and children. Too many difficulties are inherent in the study of mistaken diagnoses to permit of anything less than a complete review of each case, if the results are to have any value. The chief of these difficulties is, What is a mistake?

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* From the Department of Pediatrics, Cornell University Medical College.

1. Cabot, R. C.: A Study of Mistaken Diagnoses, J. A. M. A. **33**: 1343 (Oct. 15) 1910.

The following cases illustrate this:

A child was brought in and the diagnosis was bronchopneumonia. Clinical and roentgen-ray evidence was complete. Necropsy findings showed, however, that in addition to the bronchopneumonia there was also a hydronephrosis of one kidney, which had never even been suspected because the urinary findings were no more than one would expect in a severe febrile condition.

A boy, aged 6 years, was brought into the hospital because of certain neurologic changes. He was examined by several neurologists, but no definite diagnosis could be made. At necropsy the entire brain was as hard as though it had been in formaldehyd for three days, the only analogous pathologic condition even approaching it being the changes seen in amaurotic family idiocy.

Such cases are extremely difficult to catalogue, but it is hardly fair to demand the solution of problems which, for the present at least, are beyond the scope of a hospital, in judging its efficiency in making correct diagnoses.

Over a period of three years, 426 necropsies were done. Of these, sixty were from the obstetric service, and had not been seen by members of the pediatric staff; twenty-two were classified as unsatisfactory; seventeen patients died either in the admitting room or within twenty-four hours. Of the 327 remaining cases, the necropsy protocols agreed with the clinical diagnoses in 263 instances, or 80 per cent.

THE WRONG DIAGNOSES

Three groups stand out prominently in the mistakes, and deserve special consideration. These are prematurity, bronchopneumonia and acute intestinal intoxications. No less than sixty of the eight-one mistakes, and, for this part of the study, those cases in which the patient died within twenty-four hours are included, were in these conditions. Granting that this might be expected from mere numerical preponderance, it is no less incumbent on those in charge of infants and children to bear them in mind.

PREMATURITY

It is taught that the three essentials in the care of premature babies are to provide breast milk, to maintain body heat, and to prevent infection. All are of equal importance, but it is doubtful whether the last is given the consideration it deserves. A study of the nineteen

necropsies that did not agree with the clinical diagnoses in a series of forty-one premature infants shows that nine respiratory infections, eight cerebral or other body hemorrhages, one ulcerative colitis and a porencephalus were not recognized.

This brings out in striking fashion that the chief problem confronting the physician is the prompter recognition of respiratory infections and hemorrhagic conditions. Corollary, of course, and of equal importance, is their prevention.

That but one case of colitis was missed does not necessarily mean that the physician is less likely to overlook this condition, although this is undoubtedly true, as demonstrated in the difference between the mortality due to gastro-intestinal diseases and that due to other diseases. With breast milk available, the former are kept at a minimum, but to care for the latter requires the strictest sort of aseptic technic on the part of both physician and nurse, with the complete elimination of all visitors. Of the three essentials, it cannot be gainsaid that the infections loom large in the picture.

The overlooking of eight hemorrhagic conditions in premature infants focuses attention on a situation which fortunately is attracting the attention it deserves. Cerebral and other hemorrhages occurring in the course of protracted labors have held the center of the stage too long, and it is encouraging to note the studies that are appearing in the literature dealing with this particular problem.

One cannot but agree with Ehrenfest's [2] plea for the recognition of the fact that the prophylaxis of intracranial hemorrhages in the new-born concerns most of all the obstetrician. One should not minimize the importance of what one conceives to be the duty of the obstetrician, but that there is another side to the question, and a vastly important one, is evident. When in a series of forty-one necropsies on premature infants, there were eight brain hemorrhages that were not even suspected, it is high time to take stock of the situation.

It does not seem possible that physiologic trauma is so frequently at fault in the premature infants, even admitting that it is possible in a spontaneous delivery to have this of such force as to cause a laceration of the dura mater.

2. Ehrenfest, Hugo: The Causation of Intracranial Hemorrhages in New-Born, Am. J. Dis. Child. **26**: 503-514 (Dec.) 1923.

BRONCHOPNEUMONIA

Respiratory infections form the second large peak of mistaken diagnoses. Of the eighty-two clinically diagnosed cases of bronchopneumonia that came to necropsy, it was not present in eight, and of these three were premature infants. With this disease, the difficulty was to recognize complications. The complications that were missed were: empyema, four; general miliary tuberculosis, four; suppurative meningitis, three; peritonitis, one; double mastoiditis, one; hypertrophied thymus, one; hydronephrosis of kidney, one.

Why were these complications missed? Probably the greatest single factor was the age of the patient. The younger the infant, the more rapid was the development of the complications, frequently with an utter absence of the signs and symptoms by which it might have been recognized. With a single exception, all in this group were under 1 year, and half of them were under 4 months of age.

The missed cases of general miliary tuberculosis require a special word. Under 2 years of age, by far the great majority of these cases are diagnosed by a positive tuberculin test and a roentgenogram of the chest. One of the fundamental truths in the use of tuberculin skin tests is that in a certain percentage of overwhelming infections the reaction is negative. This happened in three of four cases, and was directly responsible for the failures.

The missed peritonitis cases demonstrated, as did the empyemas, the insidious way in which suppurative processes proceed in early infancy, without giving any hint of their presence.

In the pneumonia series there was one case of an enlarged thymus in an 11 months old infant. This suggests the interesting question as to the part that status lymphaticus plays, especially in the so-called fulminating pneumonias.

It is more than likely that a fairly large percentage of the pneumonias that progress rapidly to a fatal termination within forty-eight hours of the onset are of this type. The association of status lymphaticus with sudden death is familiar. What, perhaps, is not taken full cognizance of is the fact that there must be certain children who are in a recessive stage, and while the onset of an acute infection may be no different than in

the average child, yet the course of that infection may be so modified that a marked virulence is attributed to the infecting organism while, as a matter of fact, the host itself is primarily responsible.

ACUTE INTESTINAL INTOXICATIONS

As in the respiratory group, the difficulty was the prompt recognition of complications. The outstanding feature of the necropsies in these cases that were missed was the overwhelming preponderance of lung infections, no less than thirteen presenting such demonstrable pathologic changes. Eleven of the patients had bronchopneumonia, one a pyopneumothorax, and one a hilum tuberculosis.

If it is argued, and the argument is sound, that most of these are terminal infections, yet none the less must we recognize that our problem is twofold. Not only must immediate remedies for the presenting phenomena of dehydration be instituted, but the high incidence of respiratory infections must constantly be borne in mind. Every measure must be taken to prevent such developments.

The question as to how many of the intoxications were secondary to a parenteral infection is an open one. The majority in this series were not, although it must be remembered that many infections tend to disturb the water balance of the body.

PYLORIC STENOSIS

The differential diagnosis of pyloric stenosis does not ordinarily cause much concern, especially if we admit the contention of many that spasm is always present. Of the three cases so diagnosed which necropsy proved wrong, two were congenital abnormalities, and one presented no evidence of any obstruction. Unfortunately, the two patients with congenital abnormalities died before any roentgen-ray reports were available; and as one of these cases was diaphragmatic hernia, it was particularly unfortunate from a diagnostic standpoint.

The majority of patients with pyloric stenosis seldom vomit before the third week, and, conversely, the congenital abnormalities begin before that time. But, and this is what makes the differential diagnosis of vomiting cases in the first weeks of life difficult, a certain percentage of the malformations give signs of intermittent

obstruction. Two in our series, one a diaphragmatic hernia and the other a malrotation of the colon, were typical. The lesson to be learned from these necropsy reports is that, in every vomiting infant, it is of paramount importance to rule out a congenital malformation.

MISCELLANEOUS

There were isolated cases in which mistakes had been made, such as a failure to recognize multiple lung abscesses in an infant who had a severe suppurative adenitis of the neck; but these do not lend themselves to any particular study, because they were too few. The outstanding feature of them all was not the failure to make a correct original diagnosis, but the absolute missing of the complications.

CONCLUSIONS

1. Eighty per cent. of cases coming to necropsy in which the patients had been at least twenty-four hours in the hospital had been fully and correctly diagnosed.

2. The three groups that showed the largest percentage of error were prematurity, bronchopneumonia, and acute intestinal intoxication.

3. Complications develop so insidiously, especially in infants, that it is the failure to recognize them that leads to the greatest number of diagnostic mistakes.

4. In the differential diagnosis of pyloric stenosis, the possibility of congenital abnormalities must be fully considered.

39 East Sixty-First Street.

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TARSAL SCAPHOIDITIS

(KOEHLER'S DISEASE)*

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Tarsal scaphoiditis (Koehler's Disease)[1] is rarely mentioned in pediatric textbooks. The literature contains at least sixty-four references to this condition (Alberti).[2] As the disease affects children between the ages of 4 and 9 years, it is of special interest to the pediatrician.

In 1908, Koehler described a hitherto unobserved disease, which occurred in children between the ages of 5 and 9 years. The clinical symptoms are limping, pain, tenderness, swelling and redness over the inner dorsal surface of one foot. A roentgen-ray plate shows definite changes in the scaphoid bone and these changes are similar in all cases. The scaphoid is diminished in size, the outline is irregular, the contour, instead of being clear cut is blurred and irregular-and there is a decided increase in density due to an abnormal calcium content. The prognosis is excellent although the length of time for full recovery may be two years. Roentgenograms taken later show a fully and perfectly developed scaphoid. The treatment is immobilization in a plaster cast. In Koehler's original three cases there was no trauma.

This case history follows closely his original description.

REPORT OF CASE

History.—W. F., a boy, aged 5 years, was noticed one afternoon by his nurse while bringing him in from play to be limping. Inquiry developed the fact that his right foot hurt him and on reaching home distinct swelling, pain, tenderness and redness were present over the inner dorsal surface of the right foot. There had been no injury, although the boy thought that he might have hurt it while climbing a tree. He was put to bed, hot applications were applied and the next day most of the swelling had disappeared. He had a fever of about 102 F., and after four days observation his physician decided that the cause was acute rheumatic fever. This decision was made probably because of an indefinite history of growing pains during the preceding two months and the acute attack.

* From the Department of Pediatrics, Cornell University Medical College.

* The utter fallacy of calling a disease by name is well illustrated in this instance. Koehler has also described another condition affecting the metatarsal bones which has been tagged with his name. Anyone interested in looking up the literature must bear this in mind as it is likely to lead to confusion.

1. Koehler, A.: Ueber eine bisher Unbeachtet gebliebene Erkrankung gewisser Lendlicher Knochen, Muenchen. med. Wchnschr. **37**: 2023, 1908.

2. Alberti, D.: La sindrome scafoidea del Koehler, Radiol. med. **9**: 213-233, 1922.

Fig. 1.—Definite changes in the right scaphoid; compare with normal left scaphoid.

involving the right ankle. At this time a soft systolic murmur was present over the pulmonic area, which it was agreed was functional in character. After the patient spent three weeks in bed there was marked improvement, when a recurrence of the symptoms set in. Fortunately these subsided quickly.

For the next four months the boy was kept in bed and not allowed to put any weight on the foot. When seen at this time there was atrophy of the right leg, fulness and tenderness over the dorsum and internal part of the right foot and limitation of extreme dorsal flexion, abduction and adduction. The

panied by a vomiting spell. He was unusually well developed, being above the average in height, weight and mentality. The Wassermann and Pirquet tests were negative. The blood picture showed no abnormal changes and the serum calcium was 11.5 mg. Roentgen-ray pictures of the hands and patellae showed no abnormalities.

Fig. 3.—The perfectly developed and normal appearing right scaphoid one year later.

ETIOLOGY

Before considering the interpretations which have been offered in explanation of this condition, we must recall that the tarsal scaphoid is the last bone of the foot to ossify. This usually occurs between the age of 3 and 7 years. It is also well to remember that it not infrequently has a bilobed nucleus, and that from its keystone position in the bony framework of the arch it is extremely liable to compression.

Proehlich's[3] admonition, to be extremely careful to make a comparison with the healthy side should be emphasized. He notes that during the period of growth the scaphoid frequently assumes the form considered radiologically as characteristic of Koehler's disease. The double (scaphoideum bipartitum) or even a small accessory nucleus, which may join later to the larger one or remain completely isolated, makes it doubly important in our interpretation of the plates and warrants every bit of the stress which he places on it.

Following Koehler's article case reports began to accumulate. Schultz[4] presented seven cases, and said that they were all compression fractures. During the process of healing the nucleus of the scaphoid decreased, the contour became irregular, the structure blurred and the calcium increased. He claimed that there was a stage in which it could not be distinguished from Koehler's picture. Especially, he noted, if the demolition is small, the greater will the resemblance be to the picture originally described by Koehler.

Koehler's[5] answer to this was very definite, as an examination of the respective titles to their papers will show. He analyzed the twenty-six cases which had thus far been reported, showing that in two-thirds of the cases there had been no history of trauma, that in ten, the changes were bilateral and that in two there were analogous changes in the patellae.

It may be here mentioned that one of the three original cases showed changes in both scaphoids and both patellae. This bilateral element naturally led to the wildest theories as to the origin of the disease, Koehler himself suggesting the possibility of a central nervous pathology. Schultz's explanation of the bilateral cases was that they were simply growth varieties, but Koehler maintained stoutly that while this explanation of the double sided changes was attractive yet it could not account for the clinical picture and added further that, "Every roentgen-ray man of experience knows that, in cases of normal ossification of bone nuclei, there are pictures which show regular divided demolition and condensation which have nothing to do with trauma or are otherwise to be considered pathologic as for instance the trochlear nucleus of the humerus and the nucleus of the calcaneus."[6]

This bilateral element has gradually faded out of the picture because with an increasing number of cases it has not attracted attention appar-

3. Proehlich: [illegible]

4. Schultz, J. G. P.: [illegible]

5. Koehler, A.: [illegible]

ently because it occurs infrequently. It is to be regretted also that many of the case reports have failed to include statements regarding the patellae.

Moffatt [6] offers perhaps the most conclusive evidence that a compression fracture is not always the cause. In one of the four cases reported by him he was fortunate enough to secure a roentgenogram taken immediately after the injury to which the disease was traced. This revealed a foot normal in every respect, thus ruling out a direct compression fracture as the cause of the appearance in the roentgenogram.

Trauma plays an exceedingly interesting and perplexing part. There are very definite reports where a direct injury was the cause but strangely, the disease seldom starts directly after the trauma. McClure [7] had one case which did not show symptoms for six weeks, while Haenisch [8] reports one where a whole year had elapsed before the symptoms showed.

Preiser [9] offers a very ingenious explanation. Drawing an analogy from Kienbock's traumatic softening, following fractures of the semilunar bone, which he believed to be a nutritional disturbance following blood vessel injury, Preiser attributes the tarsal scaphoiditis to compression of that bone, as determined by the condensation in the roentgen-ray plate, leading to injury of the blood vessels and subsequent nutritional disorder in the growing bone.

Fassett [10] thinks that tuberculosis may be responsible for the picture. To accept this view we are to think of the bone as having gone through the stage of repair to the point of cicatrization without having any attention called to it, when suddenly trauma breaks down the sclerosed bone causing pain. The course of the disease, the consistently negative tuberculin tests and the general healthy condition of the great majority of the children reported, make this seem unlikely. This holds equally true for syphilis.

Pfahler [11] and Hetzel [12] agree that the condition is probably an

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6. Moffatt, B. W.: Isolated Disease of the Scaphoid, J. A. M. A. **80**:87-90 (Jan. 13) 1923.

7. McClure, C. R.: Isolated Disease of the Scaphoid, J. A. M. A. **71**:1360 (Oct. 26) 1918.

8. Haenisch, G. F.: Ueber eine häufige bisher anscheinend unbekannte Erkrankung einzelner kindlicher Knochen, München. med. Wchnschr. **55**:2377 (Nov. 17) 1908.

9. Preiser, G.: Zur Frage der typischen traumatischen Ernährungsstörungen der hurzen Hand und Fusswurzelknochen, Fortschr. a. d. Geb. d. Röntgenstrahlen. **17**:360, 1911.

10. Fassett, F. J.: Isolated Disease of the Scaphoid, J. A. M. A. **62**:1155 (April 11) 1914.

11. Pfahler, G. E.: Isolated Disease of the Scaphoid Bone of the Foot in Children (Koehler's Disease), Surg., Gynec. & Obst. **17**:625 (Nov.) 1913.

12. Hetzel, W. B.: Isolated Disease of the Scaphoid Bone of the Foot (Kochler's Disease). Am. J. Orthop. Surg. **15**:214 (March) 1915.

inflammatory osteitis or osteochondritis. The former states that the abrupt appearance and disappearance would suggest rheumatism but no other joints have been involved. Bernstein's [13] case is suggestive of a rheumatic infection. Without a plate one would naturally be inclined to attribute the clinical picture to such an infection, but the roentgen-ray findings, the invariable involvement of the same bone and the absence of infection in other joints should lead us into other channels.

Mouchet and Roederer [14] state that there is no mystery connected with the pathology. Their intensive studies of a series of roentgen-ray plates of one case made them feel sure that they were dealing with a fracture in the beginning, a compression fracture. "But" they add, "If a study of the roentgen-ray plates suggests a fracture, a consideration of the clinical course makes it necessary for us to consider it as a pathologic fracture. Trauma is never constant enough to play an important rôle, but it is probably preceded by a special condition of the bone which we designate as a dystrophy. What the nature of this dystrophy is we do not take it on ourselves to answer entirely. We shall confine ourselves to recalling the analogy that tarsal scaphoiditis presents with the osseous dystrophies seen in adolescence, as coxa vara."

COMMENT

From the numerous cases in the literature it is now possible to draw some definite conclusions. All agree that signs of inflammation are present. The disease occurs in boys in a larger percentage of cases than in girls. The right foot is more often affected than the left though there is not a marked difference. Direct trauma, such as the falling of a weight on the dorsum of the foot is seldom a factor, while indirect trauma, such as jumping from a wagon has little more weight than that usually given to the various bumps and falls which infants and children have.

It is very likely that repeated slight injury, such as occurs from constant jumping and landing full on the flat part of the foot sets up an inflammation in the growing scaphoid, provided there has been some delay in the development of the nucleus of that bone.

There can be no question that direct compression fracture will produce a similar pathologic change, and it would be splitting hairs to deny that they are cases of tarsal scaphoiditis. On the whole, however, the majority of these cases are not caused thus.

With the very definite evidence of an inflammatory process being present, it seems logical, as Mouchet suggests, to call Kohler's disease tarsal scaphoiditis.

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13. Bernstein, E. M.: Case of Kohler's Disease, Am. J. Roentgenol. **9**:315 (Aug.) 1922.

14. Mouchet, A., and Roederer, J.: La scaphoïdite tarsienne des jeunes enfants, Rev. d'Orthop. **7**:258 (Mai) 11, 1920.

SUMMARY

Tarsal scaphoiditis occurs in children between the ages of 4 and 9 years, and occurs in boys more frequently than in girls. The diagnosis cannot be made without a roentgen-ray examination. The cause may be due to repeated slight trauma to a delayed ossifying center. The symptomology and course is practically the same in all cases and the prognosis is excellent.

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CHICAGO

VITAL CAPACITY AS AN AID IN DIAGNOSIS OF TRACHEOBRONCHIAL ADENOPATHY IN CHILDREN FROM FIVE TO TWELVE YEARS OF AGE

ITS SIGNIFICANCE IN EVALUATION OF VITAL CAPACITY MEASUREMENT OF AVERAGE NORMAL CHILDREN *

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AND
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In a previous paper on the measurement of vital capacity of children, we indicated that the low values obtained by this test in some of our apparently normal subjects was probably due to tracheobronchial adenopathy.[1] The evidence in support of this view was obtained from the roentgenologic findings, in all those instances studied by this method at the time that the work was prepared for publication. The interpretation of a relationship existing between the vital capacity of the lungs and tracheobronchial adenopathy is one of considerable importance, since it implies (1) that the measurement of the vital capacity can be used as a valuable adjunct in the diagnosis of tracheobronchial adenopathy and (2) that, in the attempt to establish a standard of vital capacity for the average normal child, the incidence of this disease would materially modify the result.

At the outset, it is essential to summarize the present conception of the diagnosis, incidence and clinical significance of tracheobronchial adenopathy in children from 5 to 12 years of age, as indicated by a survey of the recent literature.

The diagnosis is considered one of great difficulty, as the physical signs are indefinite. D'Espine's sign is most generally used.[2] Its value, however, is considered uncertain, because of the discrepancy in the findings and interpretations of various investigators.[3] The roentgen-ray interpretation of hilum, root and trunk shadows is also attended by

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* From the Department of Pediatrics, Cornell University Medical College and the New York Nursery and Child's Hospital.

1. Wilson, May and Edwards, D. J.: Standards for Normal Vital Capacity for Children: The Lung Capacity in Certain Intrathoracic Conditions, Am. J. Dis. Child. **22**: 441–454 (Nov.) 1921.

2. Mach, H.: Tuberculosis of Children (translated by Dr. Mary Shelby-child), New York, MacMillan Company, 1921, p. 63.

3. Griffith, J. P. C.: Diseases of Infants and Children, Vol. 1, Philadelphia, W. B. Saunders Co., 1919, p. 330.

some uncertainty, differences in opinion being due to the variation in technic as well as to the fact that the norm for children is difficult to standardize.[4] There seems to be a general agreement that an increase in the hilum shadow is indicative of engorgement and enlargement of the intrathoracic glands, and that the accompanying extensive linear markings radiating to the lung periphery, particularly the upper parts of the lung, may be considered pathologic.[5]

As to the clinical significance of tracheobronchial adenopathy, two important facts are stressed:[6] 1. Engorgement of the intrathoracic glands accompanies and is a sequel of most infections, particularly those involving the respiratory tract, such as measles and pertussis. 2. The seat of tuberculous infection, both latent and active in children, is in the intrathoracic glands.[7] These considerations suggest that the incidence of tracheobronchial adenopathy in any group of children is likely to be high, and that the degree and permanency of the involvement will vary with the etiologic factor.

Although realizing the difficulties of any comparative study based on still uncertain criteria, as is evident from the summary of the diagnosis as outlined above, we purpose in this investigation to make a comparative study of (1) the vital capacity and roentgen-ray findings of an arbitrarily selected group of average children, apparently normal and ranging in age from 5 to 12 years, and (2) the vital capacity and roentgen-ray findings of a selected group of children with tracheobronchial adenopathy.

The subjects selected for comparative roentgenographic study and vital capacity measurement may be considered under two general groups. The first group comprises eighty-three subjects, arbitrarily selected from a total of 360 apparently normal children (who were observed in the investigation for the normal standards of vital capacity[1]). All of these children passed a routine physical examination. They were apparently healthy, and were attending public or private school in New York City. We shall subdivide this group into two divisions, one made up of fifty average white children selected without regard to race, and the other thirty-three colored children. The other main group of subjects considered in this study were selected because of predisposing history, clinical symptoms, physical signs or roentgen-ray evidence justifying the clinical diagnosis of tracheobronchial adenopathy.

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4. Pottenger, F. M.: Clinical Tuberculosis, St. Louis, C. V. Moseby Company, 1922, p. 114.

5. Dunham, Kennon: Stereoroentgenographic Studies of Pulmonary Tuberculosis, Troy, N. Y., Southard Company, 1915, p. 522.

6. Fleischner, E. C.: Bronchial Lymphadenopathy, Nontuberculous, J. A. M. A. **79**:175 (July 15) 1922.

7. Fishberg, Maurice: Pulmonary Tuberculosis, Ed. 2, Philadelphia, Lea and Febiger, 1919, p. 395.

METHOD AND TECHNIC

The vital capacity measurement was determined as described in the preliminary investigations.[1] All known factors which tend to diminish the vital capacity measurement were considered, and all subjects giving evidence of such complicating factors were eliminated from this study.

A graph of the vital capacity readings of 360 average, apparently normal children, is included for comparative study (Fig. 7).

Fig. 1.—Normal subject with a grading of 1-4.

The roentgenologic examinations, with films, were supplemented by confirmatory fluoroscopic and stereoscopic examinations in the majority of cases. The roentgen ray technic used, in the main, was that described by Denham and Blackfan.[2] In a small number of cases, serial films were taken over a period of a year or more. The degree and the extent of the hilum shadow and the pulmonary markings were attri-

2. Denham, G. E., and Blackfan, Kasmir: Preliminary Report on Clinical and X-Ray Evidence in the Course of Normal Children, Tr. Nat. Tuberculosis Ass'n, 1921.

trarily graded; those indicating little evidence of increase in the hilum shadow with lung parenchyma fairly free and clear (Fig. 1) as 1 +; those showing definite increase in the hilum shadow with pulmonary markings extending midway to the lung periphery (Fig. 2) as 2 +, and those revealing extensive increase in the hilum shadow with linear markings pronounced and extensive radiating to apices and lung periphery (Fig. 3) as 3 +.[9]

Since the completion of this investigation, there has been published by the National Tuberculosis Association, a report containing an excel-

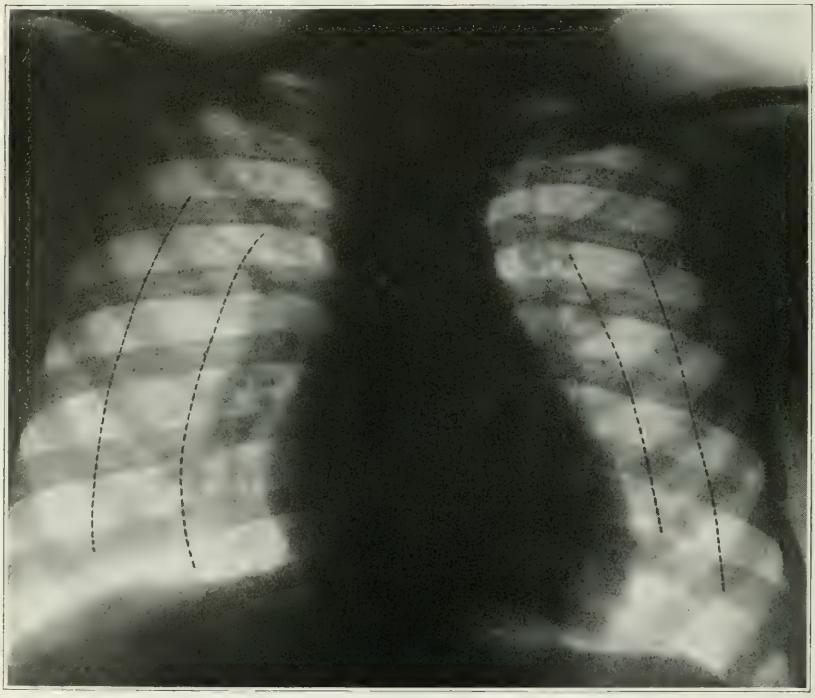

Fig. 2.—Normal subject with a grading of 2+.

lent composite diagrammatic roentgenogram of the normal chest of the child, showing a division of the lung into three vertical zones, for "convenience of description" (Fig. 5). The arbitrary divisions which we have made in our preliminary and present reports, i. e., the gradations of 1 +, 2 + and 3 +, are comparable to the division of Zone I, Zone II, and Zone III, respectively, shown in their illustration.

9. These notations were made without the knowledge of vital capacity readings, and were checked three different times by us. Likewise, many of the films were seen, and our interpretations corroborated by disinterested, competent observers.

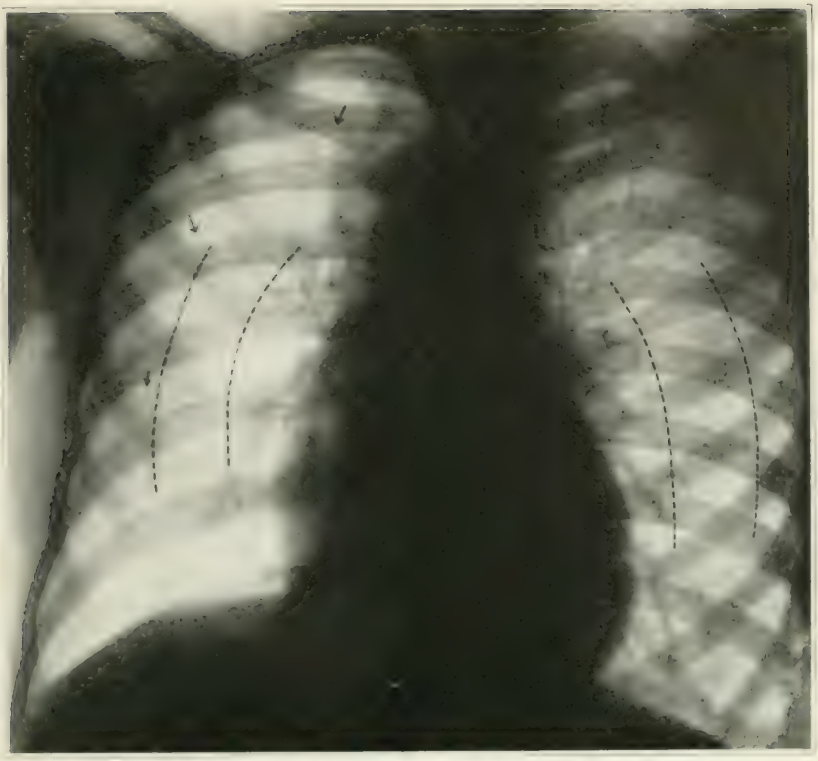

Fig. 3.—Normal subject with a grading of 3 +.

Fig. 4.—Chest of subject with tracheobronchial tuberculosis.

RESULTS

A comparative analysis of the roentgen-ray findings and vital capacity values observed for the normal group, as shown by Table 1, A and B, indicates that 16 per cent. of the white subjects and 84 per cent. of the colored subjects, with roentgen-ray findings graded as

Fig. 5.—Composite diagrammatic roentgenogram of the normal chest of the child, showing the three zones (reproduced by courtesy of the American Review of Tuberculosis).

3 +, showed average reductions in the vital capacity of 17 and 22 per cent., respectively, for each group. The remaining normal subjects, with findings graded as 2 + and 1 +, had vital capacity values within the average normal range, with slightly higher values for the 1 + group.

TABLE 1.—*Vital Capacity Readings and Roentgen-Ray Findings in Normal Subjects from 5 to 11 Years of Age*

	Roentgen Ray Grade 1 (+) Vital Capacity, Litres per Square Meters of Surface Area	Roentgen Ray Grade 0 (−) Vital Capacity, Litres per Square Meters of Surface Area	Roentgen Ray Grade 0 (−) Vital Capacity, Litres per Square Meters of Surface Area
[illegible]	1.74 1.90 1.85 1.94 1.89 1.98 1.81 2.05 1.86 2.07 1.89 1.93 1.92 2.20 1.86 2.00 2.07 Average, 1.98	1.57 1.85 1.96 1.72 1.81 1.97 1.76 1.85 1.98 1.72 1.86 2.00 1.77 1.84 2.03 1.75 1.81 2.08 1.76 1.90 2.03 1.75 1.96 2.4[illegible] Average, 1.91	1.52 1.[illegible] 1.68 1.66 1.64 1.65 1.70 1.60 Average, 1.69 (4 [illegible] of 1.[illegible])
[illegible]	1.86 2.08 Average, 1.97	1.77 1.74 1.86 1.99 Average, 1.83	1.36 1.47 1.61 1.33 1.46 1.66 1.38 1.49 1.66 1.48 1.43 1.66 1.42 1.44 1.68 1.40 1.41 1.66 1.47 1.54 1.66 1.40 1.51 1.74 1.48 1.51 Average, 1.51 (1 [illegible] of 1.[illegible])

TABLE 2.—*Roentgen-Ray Findings and Vital Capacity Readings of Thirty Subjects from 5 to 11 Years of Age, with Tracheobronchial Adenopathy*

Clinical Case	Vital Capacity Litres	Roentgen Ray Findings
Tuberculosis [illegible]	1.13 (−4.5) 1.35 (−[illegible]) 1.42 1.47 1.42 1.45	
Latent	1.58 (−1.8%) 1.61 1.66 1.68 1.70	
Nontuberculous [illegible]	1.81 (−1.8%) 1.82 1.[illegible] 1.41 1.43 1.[illegible] 1.49 1.58 1.60	Negative (−)
[illegible] group	1.43 1.47 1.46 1.47 1.4[illegible] 1.[illegible] 1.60 1.[illegible]	
	1.58 1.86	Questionable (+) Positive (+)

The individual vital capacity values are, in the main, consistent with the average values obtained. These observations are in accord with those found in the preliminary investigation.

The result of the comparative analysis of the vital capacity readings and roentgen-ray findings in our second group of subjects (those with tracheobronchial adenopathy) is shown in Table 2. The roentgen-ray findings in all but two of the subjects of the asthma group are graded 3 +, confirming the clinical diagnosis. An average reduction of vital capacity of 23 per cent. was obtained for the group. There were greater individual reductions noted, particularly in subjects with symptoms of active infection, as much as 42 per cent. in one instance. These results

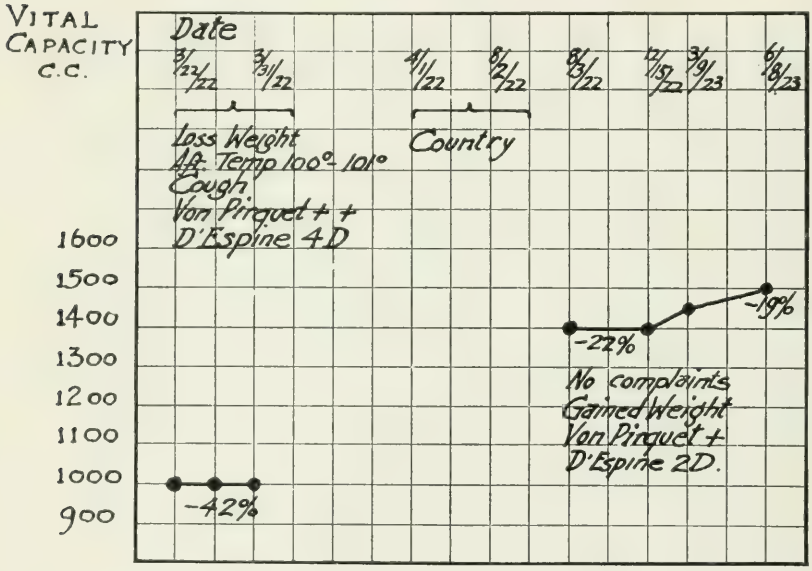

Fig. 6.—Record of vital capacity of girl (J. I., colored), 8 years of age, with tracheobronchial tuberculosis.

show a close correlation between the vital capacity, roentgen-ray findings and clinical diagnosis.

Some of the group with tracheobronchial adenopathy have been observed for a period of one or two years. The record of subject J. I. with tracheobronchial tuberculosis (Fig. 6) is of interest. It shows a reduction of vital capacity of 42 per cent. during the stage of active clinical symptoms. At periods of six months and one year later, when the condition was quiescent, the vital capacity still showed a reduction of 22 and 19 per cent., respectively. During the latter period, the child was apparently well and was attending school. Certain subjects with nontuberculous tracheobronchial adenopathy seemed to show a more

rapid increase in the vital capacity than tuberculous subjects, a few coming within normal limits within from three to six months.

A comparative analysis of the plotted curves of combined vital capacity readings for subjects graded as 1+, 2+ and 3+, and the curve of vital capacity readings of 300 average normal children (Fig. 6) is of interest. It shows rather strikingly that subjects with a grading of 1+ and 2+, respectively, fall within the normal range, 1.74 and 2.14 liters per square meter of body surface, while subjects with a

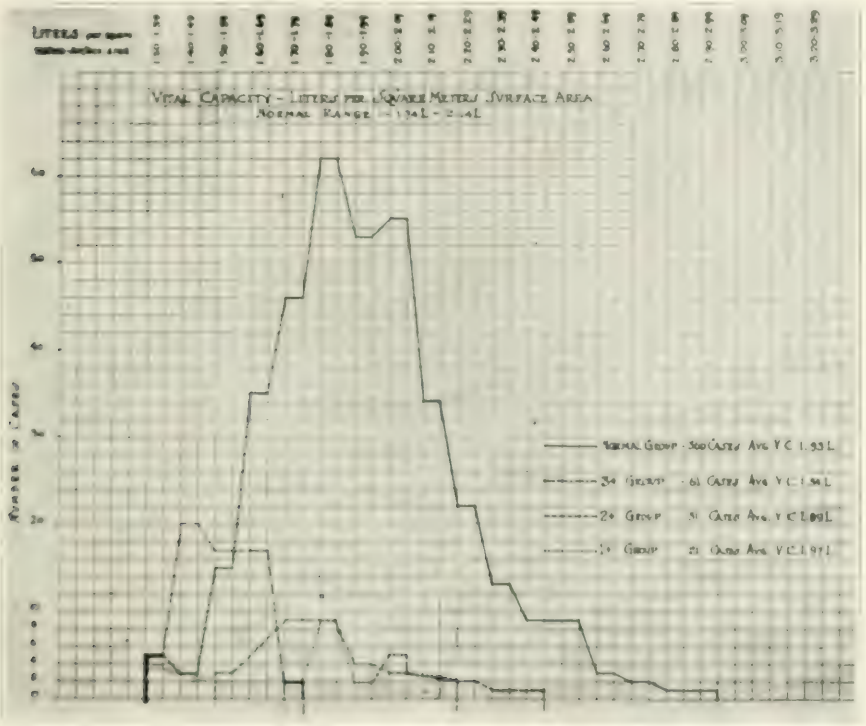

Fig. 7.—Comparative vital capacity curves of 300 average normal subjects, and subjects with tracheobronchial adenopathy.

grading of 3+ cover the lower range of the normal curve, from 1.30 to 1.69 liters per unit of body surface.

COMMENT

We have attempted to contrast the vital capacity readings and the roentgenray findings obtained from a study of average children, apparently normal, with similar observations on subjects with clinical symptoms or physical signs of tracheobronchial adenopathy. We will first consider the results of our observations on normal subjects.

The most significant feature of these results is the roentgen-ray findings observed in 16 per cent. of normal white subjects and in 84 per cent. of colored subjects. The roentgen-ray findings described in these apparently normal children, which we have graded as 3 +, may be considered as pathologic. An explanation of the failure to eliminate these subjects from the normal group by anamnesis and physical examination may be found in the unreliability of a history, and the recognized difficulty of eliciting diagnostic physical signs of tracheobronchial adenopathy, as well as the frequent absence of these signs. Of clinical significance is the reduction of vital capacity obtained for the subjects graded as 3 +, averaging 17 per cent. for the white subjects and 23 per cent. for the colored subjects. These findings indicate that, among a group of apparently normal children, one may expect to find a certain percentage of subjects who will show a diminished vital capacity, and will give accompanying roentgenologic evidence of tracheobronchial adenopathy. This would seem to be particularly true of colored subjects, possibly because of their susceptibility to such infections as tuberculosis.

A further consideration of the roentgen-ray findings in normal subjects giving vital capacity readings within normal limits lends additional support to the conclusion that the shadows observed, and graded as 1 + and 2 +, respectively, are to be interpreted as within the normal range. This view coincides with the findings reported by the National Tuberculosis Association, previously referred to.

Of clinical significance is the close relation between the roentgen-ray findings and the vital capacity readings of these subjects. This is well brought out by a comparison of the superimposed curves of combined vital capacity readings (Fig. 7). They show that subjects with a grading of 3 + cover the lower range of the normal curve, indicating that these individual low vital capacity readings may be due to tracheobronchial adenopathy. The fact that subjects with a grading of 1 + and 2 + fall within the normal range indicates, we believe, that the roentgen-ray findings have no bearing on the vital capacity measurements. These considerations make it possible to predict with reasonable confidence that apparently normal children revealing a vital capacity reading within normal limits will present, by roentgen ray, a normal picture according to currently accepted standards; and that children exhibiting a diminished vital capacity will show (other factors known to diminish the vital capacity being excluded) roentgenographic evidences of tracheobronchial adenopathy.

Our observations of the group with clinical symptoms and physical signs of tracheobronchial adenopathy are of interest in that they show a close relation between roentgen-ray findings, vital capacity and clinical diagnosis. The vital capacity measurement is of clinical significance,

therefore, in that it affords corroborative evidence concerning the clinical course and the diagnosis. Of interest are the low individual vital capacity values observed in the group with symptoms of active infection. Though the number observed is too few for any final conclusions, these observations tend to indicate that a reduction of vital capacity in subjects with tracheobronchial adenopathy of more than 25 per cent. is suggestive of an active infection; while a reduction of vital capacity in similar subjects of from 15 to 25 per cent. is suggestive of a healed or latent infection. While in no way may the diminished vital capacity observed indicate the etiologic factor, these observations support the view that a reduction of vital capacity of more than 15 per cent. supplies corroborative diagnostic evidence of tracheobronchial adenopathy.

Since at the present time the pathology underlying the roentgen-ray findings observed is inconclusive, any explanation as to the diminished vital capacity observed is speculative. However, if we consider the shadows observed as caused by connective tissue changes, due to either tuberculous or nontuberculous infection, healed or active, it is reasonable to assume a loss of lung elasticity, which may be expected to reduce the vital capacity measurement. To substantiate this assumption, extensive observations controlled by careful necropsy would be necessary. Such a study is not possible in children, but it has seemed practical in animals, and we are undertaking such an investigation.

SUMMARY

1. Diminished vital capacity and roentgenologic evidence of tracheobronchial adenopathy were found in 16 per cent. of apparently normal white subjects, and 84 per cent. of apparently normal colored subjects.

2. A reduction of vital capacity of more than 15 per cent. in an apparently normal child indicates the necessity of a roentgenologic examination.

3. The possible presence of tracheobronchial adenopathy must be considered in the evaluation of the vital capacity measurement in apparently normal children.

4. A reduction of vital capacity of from 15 to 42 per cent. was found in children with tracheobronchial adenopathy.

5. The vital capacity is an aid in the diagnosis of tracheobronchial adenopathy.

RHEUMATISM: ITS MANIFESTATIONS IN CHILDHOOD TODAY

TONSILLECTOMY IN ITS RELATION TO THE RECURRENCE OF RHEUMATISM *

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AND
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NEW YORK

There has been a decided advance in pediatrics in the last twenty-five years. Many of the diseases of infancy and childhood occur with less frequency and diminished virulence. This progress has been due to many factors, among them the development of preventive medicine and hygiene, and the important results of laboratory investigations and methods.

What influence, if any, have these factors had on the clinical course of rheumatism? What influence, more particularly, has the recent increase in tonsillectomies had on the recurrence of rheumatic manifestations? These considerations have suggested a comparison between the classical description of rheumatism in children given by Cheadle [1] about thirty-five years ago, and rheumatism as it is seen today both in England and in this country. What are the manifestations of rheumatism today and what are their relative incidence? These are some of the questions we have attempted to answer in this study.

Our material consists of 185 patients who have been under our observation for a period averaging three years; of these, twenty-five have been our patients for six years. Of the 185, 71 per cent are girls, and 29 per cent boys. In order to study our cases from the onset of rheumatic manifestations, we have given due con-

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sideration to the data gathered from past histories; by careful questioning we have attempted to reduce the evident sources of error to a minimum. Our findings coincide with the experience of others that girls are more than twice as subject to rheumatism as boys, although the contrary holds good in adult life. We observed 173 of our patients between the ages of 5 and 14; ten between 3 and 5, and only two below 3. In many of them the first manifestations of rheumatism had occurred before they came under our observation. The incidence of the ages at which rheumatic manifestations appeared is shown in Figure 1. This chart is similar to the one published by Poynton [2] in England. It is of interest to note that rheumatism occurs in the very first years of life, and that it makes its earliest appearance most frequently from 4 to 9 years of age, reaching a high maximum at 5. The earliest onset of our series was at 1½ years of age. Poynton's chart shows the maximum at 7 years of age.

Practically all of the children, and 58 per cent. of their parents, were born in the United States, which on the whole indicates a relatively good standard of living. Indeed, in 84 per cent. of our cases living conditions were exceedingly good. In the remaining 16 per cent. the rooms were dark, damp, overcrowded and dirty; the food was poor and the children showed lack of care. The majority of the children came from the west side of the city, between Fortieth and Sixty-Fifth streets, most of them within two or three blocks of the North River. This district is swept by cold winds. A study of the incidence of rheumatism in the various districts of New York for the year 1921-1922 reveals that the smallest percentage of rheumatism occurred in the districts lying farthest from the river fronts, with a progressively increasing percentage in the districts approaching the river fronts.[3] In England, likewise, the incidence of rheumatism has been found to be greatest along river fronts and buried rivers. In order to determine the seasonal incidence of rheumatism, an analysis was made of the case histories during the year 1922. This showed that 31 per cent. of the rheumatic manifestations occurred in winter, 33 per cent. in

2. Poynton, F. J.: Acute Rheumatism in Children, Lancet **2**: 1086 (Nov. 27) 1920.

3. Unpublished Report of Committee on Cardiac Classes, Association for the Prevention and Relief of Heart Disease, and the Cardiac Committee of the Public Education Association.

spring, 29 per cent. in summer, and only 7 per cent. in the fall. The summer of the year 1922 was an unusually rainy one.

The familial tendency of rheumatism is indicated by the fact that 40 per cent. of the patients had rheumatic parents, and 28 per cent. rheumatic brothers and sisters.

RHEUMATIC MANIFESTATIONS

The following rheumatic manifestations have been observed:

1. *Growing Pains, Joint Pains and Myositis.*—These conditions have been noted in 78 per cent. of the children. They are grouped together because they frequently occur in the same child, even interchangeably at times. "Growing pains" are located in the hamstring tendons, behind the knee. The children usually

state that the pain is in the thigh or calf muscles; but when they are asked to point out the exact location of the pain, their hand lies directly behind the knee. These pains may be severe enough to cause a limp, may last a few days, or may be mild and fleeting. Frequently, joint pains are complained of in the knee, hip, shoulder and phalangeal joints. They vary in intensity, may necessitate staying in bed for a short time, or may result merely in a stiffness noted on change of position, especially on rising in the morning. These joint pains and stiffness are apt to come and go, are not persistent, and may return daily or almost every day for a week or more. There are no objective signs, that is, no redness, swelling or fever, and mothers usually pay little attention to them until they learn to appreciate their significance. In this group there is included mental stiffness of a group of muscles, the striking example of which is [illegible] the more much

less frequently than growing or joint pains, and rarely in children who have not, on some occasion, had one or the other. Poynton reports torticollis preceding fatal cases of rheumatism. We have had one such fatal case.

2. *Tonsillitis and Sore Throat.*—These have occurred in 77 per cent. of our cases. This percentage includes only those cases in which there was more than one recurrence. These conditions varied greatly in intensity, and were characterized, in some instances, by a congested pharynx, with or without enlarged cervical nodes, and little fever; in others, by a frank follicular tonsillitis with high fever. The sore throat which recurred after tonsillectomy was usually of the milder type. We have observed only four cases of severe sore throat following tonsillectomy in this series. Even the mildest of sore throats may be the starting point of a rheumatic fever or of a carditis. Clinically, it is impossible to decide whether the case is one of ordinary sore throat, or whether it is the onset of a much more serious condition.

3. *Rheumatic Fever.*—This occurred in 56 per cent. of the cases, and recurred from two to six times in two fifths of them. We have classified as rheumatic fever all cases of arthritis accompanied by fever and by temporary physical changes in the joints. The relative insignificance of the arthritis is worthy of note. Usually, only one or two joints were affected; they were more often white than red, and the amount of swelling varied considerably; there were tenderness and pain, especially on active motion. In some instances the joint manifestations were so slight, or appeared so late in the course of the illness, that diagnosis was uncertain for a time. On the other hand, in a few cases we observed the adult type of rheumatism with numerous blazing joints. The course varied from a few days to a few weeks. In mild cases the fever was very slight. Severe cases were followed by a persistent characteristic pallor; this occurred in 19 per cent. of the cases, and may be considered as an indication of the virulence of the attack. The underlying anemia is difficult to combat, and improves only after months of care.

4. *Cardiac Valvular Disease.*—This was present in 69 per cent. of our cases. The remaining 31 per cent. were potential cardiac patients; that is, cases with a history of rheumatic manifestations, but without any

involvement of the heart. Of the 69 per cent., 17 per cent. were potential patients who developed valvular lesions while under our observation. Cardiac valvular disease is a manifestation, not a complication, of rheumatism. Valvular lesions in our series have followed on one or frequent attacks of other rheumatic conditions, or have seemed to be the first event in the series. In many cases the carditis was not noted, and the valvular lesion was found later in the course of a general examination for some minor complaint. From the point of view of prognosis, the cardiac involvement is the most important of all the rheumatic manifestations.

5. *Carditis.*—Sixteen per cent. of the cases developed a frank carditis under our observation. The severe cases were characterized by dyspnea, precordial pain, high temperature, and definite signs of endocarditis and pericarditis; the mild types showed a low grade temperature, a soft systolic murmur at the apex, and slight enlargement of the heart, unaccompanied by any clinical symptoms referable to the heart. These cases are frequently overlooked. We have had instances of both types of cases being followed by complete recovery without leaving any physical signs of cardiac involvement. This is most likely the condition that was present in those children who gave a history of having had heart disease and in whom, on examination, no cardiac lesions were found. Two cases in our series simply presented a definite cardiac enlargement without any endocardial murmurs. We have observed that the definite signs of cardiac failure are frequently preceded, by from two to six weeks, by a characteristic group of symptoms consisting of loss of weight, slight daily rise in temperature, increased pulse rate, fatigue, and diminishing exercise tolerance and vital capacity. The later congestive symptoms of cardiac failure, congestion of the lungs and liver, and edema of the extremities, are [illegible] in children, and occurred in only 3 per cent. of our cases.

6. *Chorea.* This condition occurred in 34 per cent. of the cases, and recurred from two to four times in half of that percentage. It is usually persistent, causes a nervous instability during the period of growth, and has a tendency to recur. The earliest symptoms noted were a definite change in the disposition of the child. The docile child becomes sulky and irritable, hard to manage, and emotionally unstable, crying and laughing

for no apparent reasons. Frequently, the child became unusually awkward, breaking dishes and dressing slowly. Persistent blinking, accompanied by an occasional grimace, shrugging of the shoulders, signs of restlessness, and mild twitching may next be observed. At this stage, the institution of complete rest would seem to abort the attack in a number of cases. In some instances the course seemed self-limited, or the symptoms becoming more severe and progressive, showing increasing incoordination of muscular activity, with complete helplessness, and loss of speach. The usual duration was from three weeks to two months. In three instances, however, it lasted from two to three years, with incomplete remissions during that time. Two thirds of the choreas were associated with heart involvement and other rheumatic manifestations. The following is an interesting illustration of the intimate association of chorea with the various rheumatic manfestations:

M. C., a girl, aged 11 years, seen in 1919, had a mitral regurgitation which was preceded by several attacks of tonsillitis and rheumatic fever. From 1919 to 1920 she had two attacks of tonsillitis. The tonsils were removed in 1920. The year following, she had a severe torticollis, shortly after this a mild sore throat, and then a severe carditis which was followed by a violent and rapidly fatal chorea.

7. *Skin Manifestations.*—These were apparent in 8 per cent. of our cases. The erythemas, urticaria, purpura and herpes zoster were all observed. To what extent these were actually rheumatic manifestations, or only associated conditions in rheumatic subjects, is difficult to determine. The only case of herpes zoster we had in our series seemed definitely rheumatic. It occurred along the eighth rib and was associated with rheumatic nodules on the scapula; there was intense pain at the location of the nodules, with none at that of the herpes.

8. *Subcutaneous Nodules.*—These were present in 11 per cent. of our cases. They are a pathognomonic sign of rheumatism, and usually of a severe, although not necessarily a fatal, rheumatism. They occur in the deep fascia, on the tendon sheaths, in the joints and over the bones. They have been noted in the occipital region, over the mastoids, over the spines of the vertebrae, along the wings of the scapulae, and on most of

the joints and bony prominences. They are usually discrete but sometimes conglomerate, and vary greatly in size, from 2 mm. in diameter or less in the majority of cases, to more than 1 cm. Seen at a certain angle, they glisten and feel like grains of rice rolling under the skin. They appear in crops, and may last for weeks or months. They usually occur in the subacute stages of rheumatic infection, but we have observed them in any stage. They have a tendency to recur. They are easily found when looked for, in thin persons, but are frequently missed in a fleshy child. When found, they confirm the diagnosis of rheumatism. The following case is of interest:

R. V., a girl, aged 10 years, was referred to the cardiac clinic by the school physician, Jan. 16, 1922. The child was pale, with a soft systolic murmur and slight cardiac enlargement, and a d'Espine to the second dorsal. The child had a past history of [illegible] sore throat, and at 9 years of age a transient stiffness and pain in the joints which lasted for three days, and which was followed by a mild chorea of a few weeks' duration. The present illness and only complaints were general fatigue, loss of weight and a slight cough. February 27, the patient returned to the clinic with a temperature of 101, acutely ill, and complaining of a persistent cough. Examination of the chest showed a d'Espine to the [illegible] dorsal. Fluoroscopic examination showed definite increase in the hilum shadow, with the heart slightly enlarged transversely. The tuberculin reaction was negative. A few [illegible] nodules were found on the knuckles and elbow. April 6, she developed a tonsilitis, followed by uneventful recovery in six weeks.

This case is of interest in that it presented the clinical picture of an active tracheobronchial nontuberculous adenitis. The presence of the nodules indicated the rheumatic nature of the infection.

Five of our twenty-one patients with nodules were potential cardiac patients, contrary to the general impression that nodules are to be found only in fatal cases of rheumatism. The remaining seven cases of nodules did occur in severe types of rheumatism with cardiac involvement; three of the cases in which there were nodules were fatal. Poynton[illegible] states that nodules may occur in cases which run a benign course, and [illegible] in patients free from heart disease.

Nodules have been considered typical of rheumatism in England, but very rare in this country. Recently, however, Brennemann [5] and Bronson and Carr [6] reported a number of cases in Chicago and in San Francisco, respectively. Our observations here would seem to show that nodules occur more frequently in this country than has usually been supposed.

Figure 2 shows several remarkably large conglomerations of nodules on the knee of a child, aged 11, with chronic cardiac valvular disease, who presented nodules at almost all the possible locations. They developed

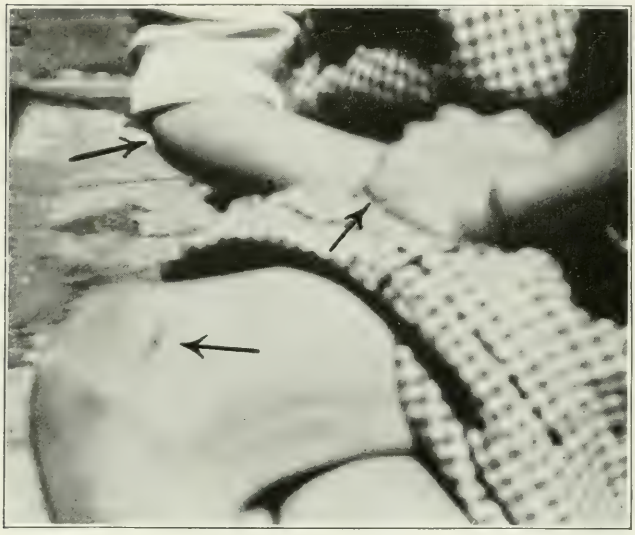


Fig. 2.—Subcutaneous nodules on knee, elbow and fingers.

during a subacute stage, about a month after a severe carditis which was fatal in five months.

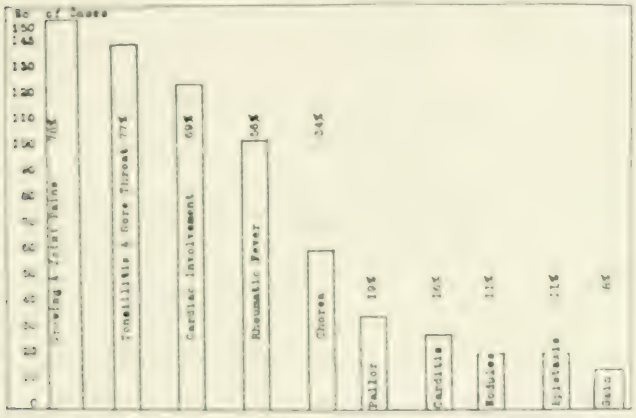
9. *Epistaxis.*—This has been found in 11 per cent. of the cases. We often found it to be associated with various acute rheumatic manifestations and, in some rheumatic subjects, to recur at certain seasons of the year during inactive periods.

5. Brennemann, Joseph: The Incidence and Significance of Rheumatic Nodules in Children, Am. J. Dis. Child. **18**: 179 (Sept.) 1919.

6. Bronson, E.; Carr, E. M., and Perkins, W. A.: Subcutaneous Fibroid Nodules in Rheumatism, Am. J. M. Sc. **165**: 781 (June) 1923.

INCIDENCE OF RHEUMATIC MANIFESTATIONS

The relative incidence of the various rheumatic manifestations is shown in Figure 3. It is of interest to compare this chart with that of Poynton,[2] published in 1920. In his chart he considered 125 patients with rheumatic fever and chorea that were observed in a hospital ward in the course of one year. His chart shows 92 per cent. with cardiac valvular disease, 88 per cent. with rheumatic fever, 83 per cent. with chorea, and 28 per cent. with nodules, as compared with 69, 56, 34 and 11 per cent., respectively, in our chart. The



differences are readily accounted for by the fact that our cases were chiefly observed in the clinics, and were, in the main, ambulatory cases. Poynton reported 28 per cent. of nodules in his group of severe cases. Our 11 per cent. in the mixed group is relatively in proportion.

Our cases fall into four groups. Of our 188 patients there were:

1. Eighty-five with sore throat, arthritis and cardiac involvement. In this group there were eight cases of nodules.

2. Twenty-six with chorea, sore throat, arthritis and cardiac involvement, among which were seven cases of nodules.

3. Fifteen with chorea and cardiac involvement [illegible] with one case of nodules.

4. Fifty-nine potential cardiac patients, nineteen with chorea and thirty-five without chorea. In this group were five cases of nodules.

The greatest percentage of nodules was found in Group 2, which likewise is the group with the greatest percentage of rheumatic manifestations.

FATALITIES

Four per cent. of our cases were fatal. In this group were seven girls and one boy. Three of these cases presented nodules. Two were fulminating first

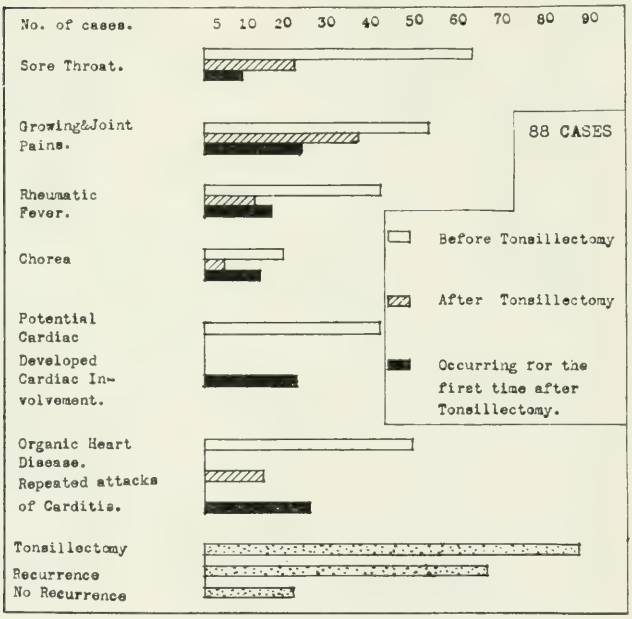


Fig. 4.—Relation between tonsillectomy and the occurrence of rheumatic manifestations.

attacks, one occurring at 9 years of age, the other at 20 months. Six were virulent terminal infections following previous attacks with recovery.

MANAGEMENT OF RHEUMATIC CHILDREN

Besides dealing with the acute manifestations of rheumatism according to accepted methods, we have treated our patients with two objects in view. First, we

have endeavored to maintain their nutrition by general dietetic and hygienic measures. Wherever possible, the child was sent to a home for convalescents in the country for a prolonged period. From our observation it would seem that the improvement in the general physical condition of the child which resulted from such care rendered the child better able to resist further infection.

On the other hand, it is necessary to get rid of foci of infection, the teeth and tonsils being those most easily eradicated. The teeth have been cared for as a routine procedure, and our experience has been that the removal of carious teeth and other dental operations had little influence on the course of rheumatism in children observed.

TONSILLECTOMY AND ITS RELATION TO THE RECURRENCE OF RHEUMATIC MANIFESTATIONS

Tonsillectomies were performed in eighty-eight of our cases. In seventy cases the tonsils were entirely enucleated, while in eighteen cases small tabs were left. Table 1 shows that rheumatic manifestations recurred in sixty-seven cases, at intervals of from one to eleven years after the tonsillectomy. In eighteen of these, incomplete tonsillectomy was done, and recurrences occurred in fourteen cases. Figure 4 shows the recurrence of the various rheumatic manifestations after tonsillectomy. Among these there were twenty-eight cases of rheumatic fever, eighteen cases of chorea, sixty cases of recurring growing and joint pains, and thirty-one cases of sore throat. Cardiac involvement occurred after tonsillectomy in twenty-two cases, and in four of our eight fatal cases of carditis, tonsillectomies were performed two years or more before death. In four [illegible] our cases, tonsillectomies were performed from two to six years before the onset of rheumatic manifestations. Table 2 shows that the remaining twenty-one cases were followed by no rheumatic manifestations; in two thirds of these, tonsillectomy was performed within the last two years. Of the eighteen cases in which incomplete tonsillectomy was performed, there was no recurrence of rheumatic manifestations in four. A comparison of the incidence of rheumatic manifestations in many cases in which tonsillectomies were performed, observed during a similar period

TABLE 1.—*Recurrence of Rheumatic Manifestations After Tonsillectomy in Sixty-Seven Cases*

Case	Age at Operation	Age at Onset of Rheumatic Manifestations	Years After Operation	Years Under Observation	Diagnosis	Rheumatic Manifestations: Before Tonsillectomy						After Tonsillectomy: 1 to 3 Years						After Tonsillectomy: 3 to 5 Years						After Tonsillectomy: 5 to 11 Years					
						Rheumatic Fever	Tonsillitis	Growing and Joint Pains	Chorea	Nodules	Carditis	Rheumatic Fever	Sore Throat	Growing and Joint Pains	Chorea	Nodules	Carditis	Rheumatic Fever	Sore Throat	Growing and Joint Pains	Chorea	Nodules	Carditis	Rheumatic Fever	Sore Throat	Growing and Joint Pains	Chorea	Nodules	Carditis
94	7	5	5	3	M. R.	0	+++	0	0	0	+	0	++	+	0	0	0	+	0	0	0	0	0	..	..	..	..	..	..
108	7	4	3	3	M. R. S.	+	+++	+	+++	0	+	0	++	+	0	0	0	0	0	0	0	0	0	..	..	..	..	..	..
101	10	12	9	4	M. R. S.	0	0	0	0	0	0	0	0	+	0	0	+	0	+	+	0	0	+	0	0	0	0	0	+
64	13	12	1	3	M. R.	+	+	+	0	0	+	0	++	+	0	0	0	..	..	..	..	..	..	..	..	..	..	..	..
163	3	3	0	2	Pot.	0	0	0	0	0	0	0	++	+	0	0	0	0	+	+	0	0	0	0	0	+	0	0	0
74	9	3	4	3	M. R.	+	++	+	0	0	0	0	+	+	0	0	+	..	.	..	..	..	..	..	..	..	..	..	..
68	4½	3½	3	3	M. R.	+	0	+	0	0	+	0	+	+	0	+	+	..	..	..	..	.	..	..	..	..	..	..	..
67	9	4	3	3	M. R.	0	+	+	0	0	+	0	+	+	0	0	0	..	..	..	..	..	..	..	..	..	..	..	..
58	14	12	1	2	M. R. S.	0	+	0	+	0	+	0	0	+	0	0	+	..	..	..	..	..	..	..	..	..	..	..	..
																	Death												
53	8	5	3	3	M. R.	0	++	+	0	0	+	0	+	+	0	0	0	..	..	..	..	..	..	..	..	..	..	..	..
45	9	4	8	4	M. R.	+	+	+	+	0	+	0	0	+	0	0	0	0	+	+	0	0	+	0	+	+	0	0	0
166	12	5	3	3	M. R. S.-A. I.	0	++	0	+	0	+	0	0	+	0	0	+	..	..	..	..	..	..	..	..	..	..	..	..
167	4	8	7	2	M. R.	0	0	0	0	0	0	0	0	+	0	0	0	+	0	+	0	0	+	+	0	+	0	0	0
182	9	5	5	3	Pot.	+	++	+	0	0	+	0	0	+	0	0	0	0	0	+	0	0	0	..	..	..	..	..	..
173	6	5	7	2	Pot.	+	+	+	0	0	0	0	0	+	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0
19	12	10	2	1	Pot.	0	+	+	0	+	0	0	+	+	0	0	0	..	..	..	..	..	..	..	..	..	..	..	..
87	9	5	3	5	M. R.	+	+	+	0	0	+	+	+	+	0	0	0	..	..	..	..	..	..	..	..	..	..	..	..
90	12	10	4	3	M. R.	0	+	+	0	0	+	0	0	+	0	0	0	0	0	++	0	0	0	..	..	..	..	..	..
91	9	5	4	3	M. R.	+	+	+	0	0	+	0	0	+	+	0	0	..	..	..	..	..	..	..	..	..	..	..	..
96	11½	7	10	2	M. R.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	0	0	++
135	12	11	2	3	M. R. S.	+	+	+	+	0	+	0	+	+	0	0	0	..	..	..	..	..	..	..	..	..	..	..	..
115	12	11	2	2	Pot.	+	+	+	0	0	+	0	0	+	+	0	0	..	..	..	..	..	..	..	..	..	..	..	..
121	10	10	3	2	Pot.	0	0	0	+	0	0	0	0	0	+	0	0	..	..	..	..	..	..	..	..	..	..	..	..
104	6	6	4	3	M. R.	0	+	+	0	0	0	+	0	0	+	+	+	+	0	0	+	+	0	..	..	..	..	..	..
117	10	8	3	4	Pot.	0	+	+	+	0	0	0	0	+	0	0	+	.	..	..	..	..	..	..	..	..	..	..	..
114	4	5	6	2	Pot.	0	0	0	0	0	0	0	0	+	0	+	0	0	0	0	0	0	0	0	0	++	0	+	0
112	10	9	3	2	Pot.	+	0	+	+	0	+	0	0	+++	0	0	0	..	..	..	..	..	..	..	..	..	..	..	..

showed recurrences in seventy-eight, and no recurrence in nineteen, as shown in Table 2. These results are very similar to those obtained in the cases in which tonsillectomy was performed, which confirms the well known clinical observation that rheumatism may be inactive for a period of years. Of twenty-five cases in which there had been the most severe rheumatism during the past year, tonsillectomy had been performed at least two years before in twelve. The patients in our series who showed most marked general improvement after tonsillectomy were ten in number. Eight of these had suffered previously from severe tonsillitis, and two had been markedly underweight.

St. Lawrence,[7] in a recent study of eighty-five tonsillectomies, in a group of rheumatic children, reports the following results: Sixty per cent. of his cases showed no recurrence of rheumatic manifestations for three and one-half years after operation, as compared with 24 per cent. of ours. Of the single rheumatic manifestations, 7 per cent. of the cases that presented sore throat before operation showed recurrence after tonsillectomy in his series, as compared with 34 per cent. in ours: of the growing and joint pains in his series 23 per cent., as compared with 70 per cent. in ours: of rheumatic fever, 16 per cent. in his series, as compared with 29 per cent. in ours. Of the choreas, his series showed 50 per cent. as compared with 28 per cent. in ours. Of fifty-eight patients with organic heart disease in his series, twelve had at least one attack of cardiac failure before the tonsils were removed, and only one patient had an attack afterward, as compared with forty-nine cases of organic heart disease of our series in which there were one or more attacks of carditis before operation in thirty-two, and recurrence after operation in fourteen. These percentages do not include the large number of cases in our series showing occurrences of rheumatic manifestations after operation which were not present before operation, as may be seen in Figure 4.

An explanation of the recurrence of rheumatic manifestations in so many cases after tonsillectomy in our series is apparent when we consider the many other possible sources of infection. While the recognized

7. St. Lawrence, William: Effect of Tonsillectomy on the Recurrence of Acute Rheumatic Fever and Chorea, J. A. M. A. **75**: 1035 (Oct. 16) 1920.

foci of infection are the tonsils, teeth, ears and sinuses, is it not possible also that the lymph nodes draining any part, once the seat of rheumatic infection, whether pharynx, joints, heart or meninges, may be, in themselves, constant foci of infection?

Recently, Irons [5] has mentioned the tissues about the hila of the lungs as a frequent focus of infection. We have observed three other cases similar to the second case cited above, in which a severe carditis was associated with an active tracheobronchial adenitis. These cases suggest that the tracheobronchial lymph nodes may play an important rôle in rheumatism, as they do in tuberculosis and in other general infections in children. With the possibility of so many other active foci of infection, it is not surprising that so many of our cases showed recurrence of rheumatic manifestations after tonsillectomy. Poynton [2] concludes from a study of the recurrence of rheumatism after tonsillectomy that "this, though a valuable operation in many cases, does not prevent further attacks. . . . Although enucleation is a preventive measure of importance, it is not a panacea for rheumatism." However, we believe that all tonsils, diseased or the seat of recurrent attacks, should be removed.

COMMENT

The manifestations of rheumatism differ in no striking way from those described by Cheadle more than a generation ago, or from rheumatism in England in late years. Rheumatism is still a protean disease. It appears in one after another of its varying manifestations, mild or severe in turn. These may follow one another in close succession, or at long intervals throughout entire childhood and into adolescence. The order in which the manifestations occur varies as widely as the time intervals. Any of the conditions that we have described may be the first or the last to appear. Rheumatism is an insidious disease, probably because of the possibility of numerous active foci. When a case is apparently inactive, a severe attack of chorea, rheumatic fever or carditis often develops. Many patients, on the other hand, do surprisingly well, especially when the critical years of puberty have been safely passed. That rheumatism is an infectious disease is now an established fact.

5. Irons, E. E.: Acute Infectious Endocarditis, Arch. Int. Med., 1913, xii, 466.

SUMMARY

In our study the following observations are worthy of note:

1. A study of the relation between tonsillectomy and the occurrence of rheumatic manifestations showed that 76 per cent. of eighty-eight cases have been followed by recurrence of rheumatic manifestations in from one to eleven years after tonsillectomy. In a control group of ninety-seven cases without tonsillectomy, studied over a similar period, 80 per cent. showed recurrence of rheumatic manifestations. Nonrecurrence of rheumatic manifestations has been observed in 24 per cent. of eighty-eight cases with tonsillectomy, and in 20 per cent. of ninety-seven cases without tonsillectomy. Of eighteen cases with incomplete tonsillectomy, 78 per cent. were followed by recurrence of rheumatic manifestations, and 22 per cent. by nonrecurrence. All of these findings suggest a consideration of other less mentioned sources of infection. Any tissue, previously the seat of a rheumatic infection, would seem to be the most obvious source or focus for reinfection.

2. Preceding the definite signs of cardiac failure by from two to six weeks we have observed loss of weight, slight daily rise in temperature, increased pulse rate, fatigue, and diminishing exercise tolerance and vital capacity.

3. An active tracheobronchial adenitis, associated with a carditis, occurred in three cases of our series.

4. Rheumatic nodules have been observed in 11 per cent. of our cases. Five instances occurred in patients with potential cardiac disease.

5. The general progress in preventive medicine and hygiene in the last twenty-five years has not seemed to influence the clinical course of rheumatism as we see it today.

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The Clinical Value of Vital Capacity and Exercise Tests in the Management of Children with Organic Heart Disease.*

MAY G. WILSON, M.D.

[illegible]

*Presented at the Seventy-fifth Annual Session of the American Medical Association, Chicago, June, 1924

CLINIC OF DR. MAY G. WILSON

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THE CLINICAL VALUE OF VITAL CAPACITY AND EXERCISE TESTS IN THE MANAGEMENT OF CHILDREN WITH ORGANIC HEART DISEASE*

IN children with heart disease a knowledge of the capacity for physical activity is of the utmost practical importance. The determination of the advent of cardiac failure, the stage of convalescence, the day of return to school, the ability to climb stairs, as well as the choice of out-door games, are some of the practical questions the physician must consider. Such information is not always available from the history and physical examination alone. This is particularly true when dealing, on the one hand, with the overanxious or non-observant mother, and, on the other hand, with the timid or fearless child.

Recent investigations have indicated the need and value of establishing some clinical standards of circulatory function or efficiency, while at the same time emphasizing the difficulty of obtaining any exact estimate of the cardiac reserve. The two most accepted clinical methods are any standardized test exercise and the vital capacity. We have in previous communications,[1, 2] on Exercise Tolerance of Children with Heart Disease described standardized test exercises and standards for normal vital capacity. The clinical value of these tests in the case of children with heart disease is the subject of today's study.

The practical application of these tests is best demonstrated in the use of the functional classification of organic heart disease adopted by the Association for the Prevention and Relief of

*From the Department of Pediatrics, Cornell University Medical College, and the Cardiac Clinic of the New York Nursery and Child's Hospital. This study has been aided by the F. S. Sturges Research Fund.

Heart Disease in use in most cardiac clinics. In the Cardiac Clinic of the New York Nursery and Child's Hospital this classification has been amplified as follows:

Class 1. Organic. (Able to carry on habitual activity):

As determined by careful history and physical examination.

As controlled by vital capacity test. (A vital capacity within normal limits.)

As checked by an exercise test: Able to tolerate an average or severe test exercise, *i. e.,* Staircase test, four flight rise of 30 feet in twenty to forty seconds. Dumb-bell test: Swing two 4, 5, or 7 pound dumb-bells twenty to thirty times, two seconds for each swing.

May be permitted to attend school, take part in all but competitive school athletics.

Out-door sports may include walking, skating, cycling, baseball, tennis.

(All exercise to be carried on well within the limits of fatigue.)

Class 2, A. Organic. (Able to carry on slightly diminished physical activity):

As determined by physical examination and history of symptoms following usual activity.

As controlled by vital capacity test: Reduction of vital capacity of 10 to 25 per cent., other factors known to diminish the vital capacity being excluded.

As checked by an exercise test: Unable to tolerate an average or severe test exercise but able to tolerate a mild test exercise, *i. e.,* staircase test, two flight rise of 15 feet in forty seconds. Dumb-bell test: Swing two 4, 5, or 7 pound dumb-bells ten to fifteen times, two seconds for each swing.

May be permitted to attend school under supervision and take part in restricted exercises. This can best be done at a Convalescent Home.

Indulge in graduated exercises and physiotherapy.

(Should report weekly for observation.)

Class 2, B. Organic. (Able to carry on greatly diminished physical activity):

As determined by physical examination and history of symptoms following habitual activity.

As controlled by vital capacity test: Reduction of vital capacity of 25 to 40 per cent., other factors known to diminish the vital capacity being considered.

As checked by an exercise test. Unable to tolerate the mild test exercise, but able to tolerate only slight exercise, *i. e.,* one flight of stairs in forty seconds.

Should not be permitted to attend school.

Is best taken care of in a Convalescent Home.

May have physiotherapy and graduated exercise.

Should have daily periods of rest and be under close observation.

Class 3. Organic. (Unequal to any physical activity):

As determined by physical examination and history.

As confirmed by vital capacity: Reduction of vital capacity of 40 to 80 per cent.

Unable to tolerate any exercise, having symptoms at rest. Must have absolute rest in bed.

This amplified classification has proved of great value in indicating to nurses, clinics, convalescent homes, social workers, and the schools the status of the case from the only standpoint in which they are interested, namely, what may the child be permitted to do. It is very important to keep in mind, however, that any classification holds for a variable length of time and is dependent upon possible further developments. As a rule, a Class I case will retain its classification until the occurrence of some further infection. It is our routine to impress the fact that after any intercurrent illness the child must return for reclassification. Cases classified 2. A or 2. B may be convalescent from a Class 3 or going on to a Class 3. In either case the child should be seen at least weekly and be observed closely, the occurrence of any clinical symptoms taking precedence over classification.

For a detailed description of method and technic of vital capacity and exercise tests used the reader is referred to the communications previously referred to. The vital capacity test is simple and practical. A spirometer is part of the equipment of most cardiac clinics. The vital capacity is taken routinely by an assistant at each visit, the entire process occupying about five minutes for each case. The use of a special chart (Fig. 43) enables a reading in percentage of normal to be recorded without any calculations.

The child is comfortably seated in front of the spirometer with head erect and shoulders back. The tube leading to the spirometer with a clean mouth-piece attached, is then held in the hand and the following steps are carried out successively and with due care:

(1) The deepest possible inspiration (breath) is taken.

(2) The mouth-piece is quickly placed into the mouth and held tightly between the lips.

(3) The breath is rapidly and completely blown into the spirometer (empty feeling).

(4) The reading of the instrument is taken and a record made of it.

The highest number of cubic centimeters recorded in from three to five successive tests is accepted as the vital capacity. The patient of about one minute should accept as many tests as required.

Chart I, A

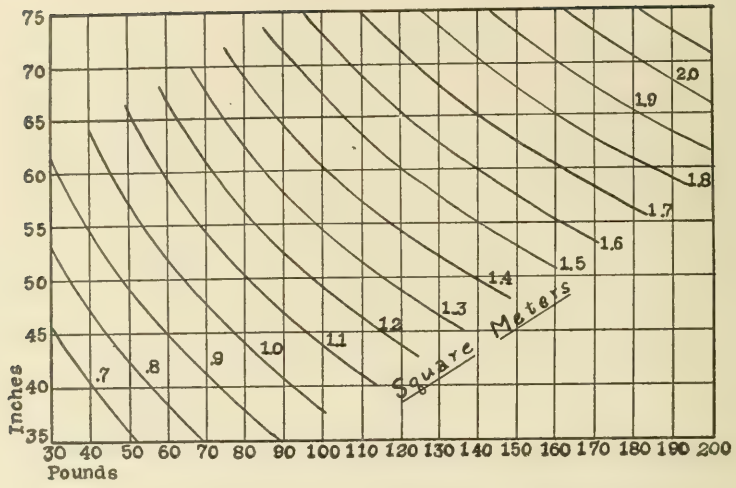


Chart for deriving body surface area from height (in inches) and weight (in pounds). Modified from DuBois chart, Arch. Int. Med. 17, 863,.

Fig. 41—The technic of vital capacity measurements on children.

Chart I, B

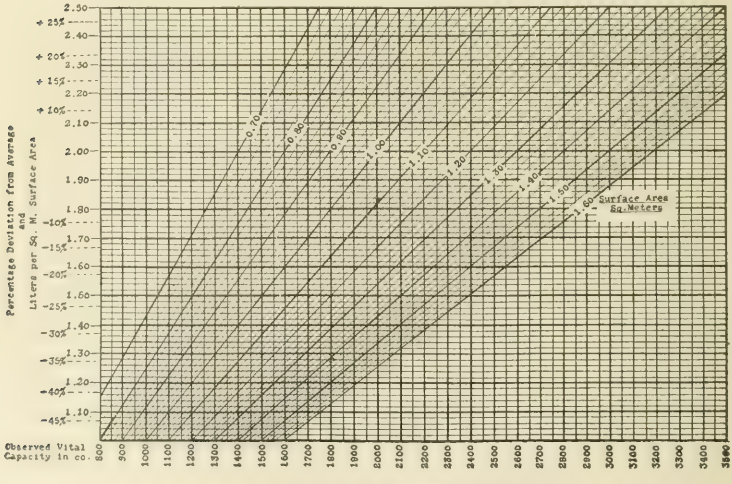

Percentage Deviation from Average and Liters per Sq. M. Surface Area
Observed Vital Capacity in cc.
Surface Area Sq. Meters
CHART FOR REDUCING THE OBSERVED VITAL CAPACITY (in cc.)
TO LITERS PER ONE SQUARE METER SURFACE AREA

Fig. 42.

Certain precautions must be observed. Only one inspiration should be taken and this should be the fullest and deepest inspiration; it should also be completely expelled. Children are likely to try too hard and fix the chest, holding the breath so that only the air in the upper passages is expelled. Or they are apt to remove the mouth-piece before the chest is completely emptied. If one is on the lookout these difficulties [illegible] with little trouble.

Directions for Using Graphic Charts

I

A. B.

(1) Obtain net weight in pounds and net height in inches.

(2) Find surface area in square meters on Chart I, A.

(*e. g.*) John: Surface area, 0.94 square miles; vital capacity, 1650 0.94 square meters.

(3) Determine vital capacity measurement in cubic centimeters.

(4) Find on Chart I, B the point of intersection of the vertical line (of the observed vital capacity in cubic centimeters) with the oblique line (of the calculated surface area in square miles). Then transpose this point of intersection to the left margin by following along the nearest horizontal line, and read the vital capacity in liters per square meter and the percentage of the normal.

(*e. g.*) John: Surface area, 0.94 square miles; vital capacity, 1650 c.c.; liters per square mile surface area, 1.76—; 10 per cent. below average normal.

The test exercises used (Fig. 43) are the staircase and dumb-bell tests. The parent or another child may assist in recording the numbers, the entire process occupying about five minutes for each case. The staircase test is particularly useful for timid children and if the parents are apprehensive. Should the child be unaccustomed to physical exercise and the arm muscles poorly developed, the dumb-bell test should be substituted by the staircase test. As a rule boys enjoy the dumb-bells.

A test exercise is considered to be tolerated if satisfactorily performed, and when on completion there is no apparent general exhaustion, although the arms may be tired. The color of the face is flushed, the respirations are increased slightly in depth and frequency, the systolic blood-pressure shows a normal curve, *i. e.*, a rise of 10 to 40 mm., with maximum readings within twenty to forty seconds and a return to normal within two minutes (Fig. 44). This is the reaction obtained with average normal children to these test exercises. Any other test exercise that makes a definite demand on the physical capacity may be substituted, provided the reactions of a sufficient number of

STANDARDIZED TEST EXERCISES

Test Exercises	Age in Years for Standard Weight and Height	Simple or Mild: No. of D.-B.	Simple or Mild: Weight, Lbs.	Simple or Mild: Swings, Times	Normal Range — Average: No. of D.-B.	Average: Weight, Lbs.	Average: Swings, Times	Normal Range — Severe or Strenuous: No. of D.-B.	Severe or Strenuous: Weight, Lbs.	Severe or Strenuous: Swings, Times
Dumb-Bell Test:										
Swinging two iron dumb-bells from the floor to full stretch of arms overhead and back again between the legs at a constant rate of two seconds for each swing	6-8	2	3	10	2	3	20	2	3	30
		2	4	10	2	4	20	2	4	30
	8-12	2	4	10	2	4	20	2	4	30
		2	5	10	2	5	20	2	5	30
	12-15	2	5	10	2	5	20	2	5	30
		2	7	10	2	7	20	2	7	30
		2	10	10	2	10	20	2	10	30

Staircase Test:	Age, Yrs.	Simple or Mild: No. of Flights	Simple or Mild: Rise, Ft.	Simple or Mild: Time, Sec.	Normal Range — Average: No. of Flights	Average: Rise, Ft.	Average: Time, Sec.	Normal Range — Severe or Strenuous: No. of Flights	Severe or Strenuous: Rise, Ft	Severe or Strenuous: Time, Sec.
Stairs taken at a steady climb without rest	6-14	2	15	40	4	30	40	4	30	2[illegible]

	Reaction of Average Normal Children Following Test Exercises: To the Mild Test Exercise	To the Average Test Exercise	To the Severe Test Exercise
Color of face (flushed)	.....	+	++
Degree of dyspnea	.....	+	++
Degree of fatigue	.....	.....	+
Rise of systolic blood pressure	10-15 mm.	20-30 mm.	30-40 mm.
Type of systolic curve	Normal	Normal	Normal

Fig. 43.

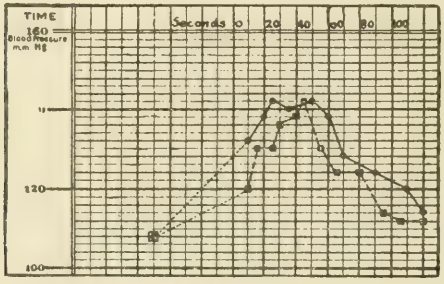


Fig. 44.

normal children are first studied and standardized for comparison. It is essential to be familiar with the general and circulatory reactions of normal children to these test exercises to

intelligently interpret the reaction of children with heart disease. It is also important to inquire as to the previous exercise tolerated, as a child mainly restricted or a convalescent cannot be expected to have a maximum normal tolerance, such as is obtained in a child who has not been restricted and has indulged in strenuous exercises. Children with a wide normal range of systolic blood-pressure, or those having a high blood-pressure give bizarre systolic curves that are difficult to interpret. This is particularly observed in the unstable, nervous child. However, in our experience, these cases have been in the minority. Many of the children have been tested over a period of years and have shown remarkably constant reactions. There need be no fear in giving a child with heart disease a test exercise. We have only observed one case in which there was an apparent collapse, attributed at the time to the test exercise. She, however, had a similar collapse on being told to enter the hospital. It was also learned that, in order to have her way at home, she would with very little effort suddenly tremble, grow pale, perspire, and faint. However, a test exercise should never be given to a Class 3 case or to a case with a recent carditis for at least two weeks after a normal temperature. If a diminished tolerance is expected, a mild test exercise should be always the first one given.

A test exercise is considered not to be tolerated if during the exercise or at the completion there is undue exhaustion or delayed recovery. The respirations are rapid, shallow, and labored. The face is pale and there may be profuse perspiration. The systolic blood-pressure curve is abnormal, i. e., an initial fall, or a slow rise of 20 to 30 mm. with maximum readings delayed or prolonged fifty to one hundred and twenty seconds or more, with a return to normal delayed three to six minutes. This is the reaction to a test exercise which is tolerated by normal children, and it is similar to the reaction obtained in normal children who have been given a greater amount of exercise than they have been able to tolerate (Fig. 4). The degree of the general and circulatory reactions to the particular test exercise classifies the case as 2 A or 2 B. In analysing the

systolic blood-pressure curve it is essential to consider the fall or rise, amount of rise, and return to normal, as well as the time of maximum readings, before designating the curve as normal or not. Frequently a delayed return to normal will be the first indication of an abnormal curve; a slight increase in work will bring out a delayed rise or prolonged summit. The blood-pressure curve is an excellent check on personal observation of the general reaction. A record of the reaction to a previous test exercise is of great value for comparison. As a general rule, we do not follow the pulse after exercise, as it requires a trained assistant, who is not always available.

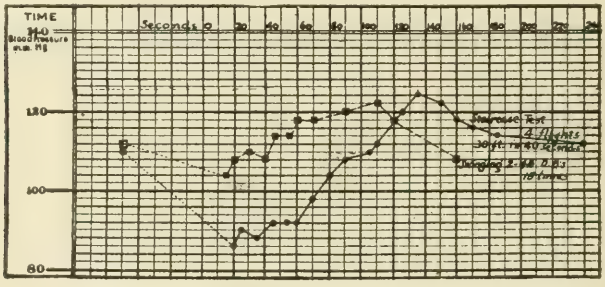


Fig. 45

In a previous paper we have shown that the vital capacity measurement may be accepted as a substitute for an exercise test, provided all other factors known to diminish the vital capacity have been excluded. The vital capacity test may be used for all types of cases, and particularly adapted for bed cases (Class 3). As a rule the vital capacity within normal limits indicates a normal exercise tolerance, and a test exercise may be omitted. A reduction in vital capacity of 10 per cent. or more must be checked by an exercise test because of the possibility of the presence of other factors which may diminish the vital capacity. Once a normal vital capacity has been recorded, subsequent readings will be found to closely follow and indicate the clinical course. Here, as with exercise tests, due consideration must be given the expected normal range for the individual case, since a child accustomed to strenuous exercise

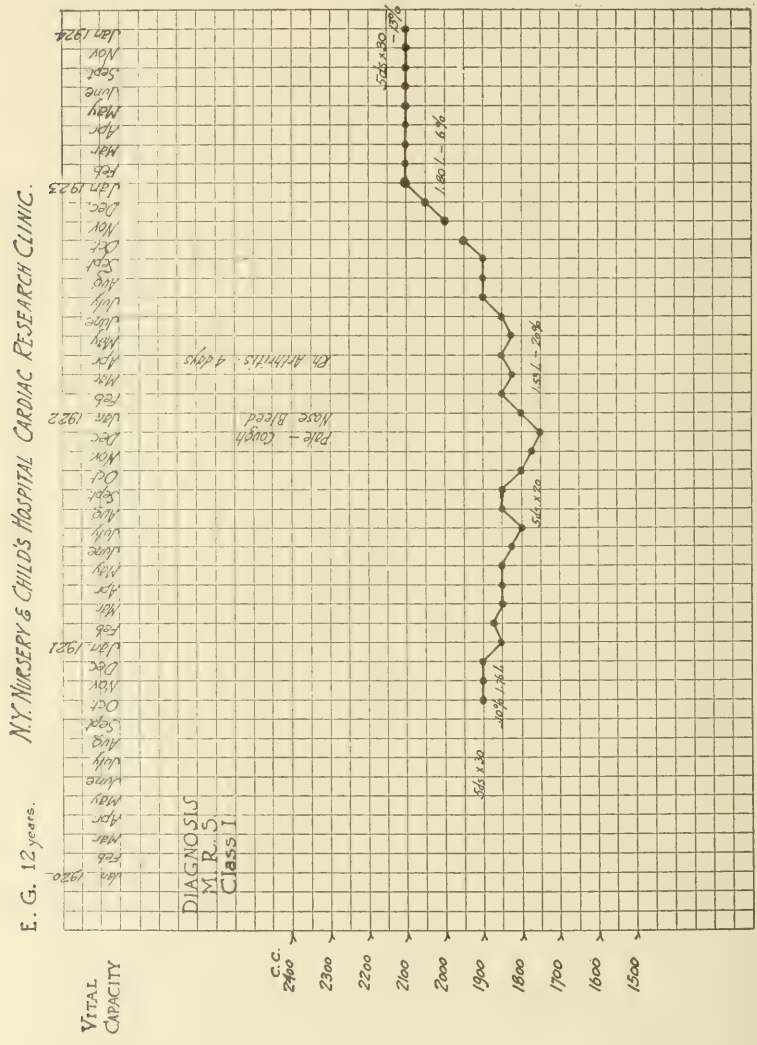
may be expected to have a higher normal than one who has been restricted, and slight reductions have more or less significance. Daily vital capacity readings are useful in following up the therapeutic action of digitalis.

A diminished exercise tolerance, as indicated either by a gradual increasing reduction in vital capacity or a diminishing tolerance for test exercise, has been observed in many cases to precede the advent of the definite signs of cardiac failure by from two to six weeks. It is, as a rule, not associated with definite complaints from the child, but may be associated with some loss of weight, increase of pulse-rate, and a slight temperature.

The use of the exercise test and vital capacity as an index of the tolerance to other forms of exercise has been to some degree empiric. A practical demonstration of the validity of this assumption has been the close agreement that has obtained between the clinic classification and the ensuing course of the case. For the past four years 125 children have been classified in the clinic and segregated in special cardiac classes in the public schools of New York City. These children have been observed daily from 9 to 5. Their activities indoors and out have been closely observed and recorded; these school reports, including weight, temperature, and pulse readings, have been filed in the clinic. With this close follow-up we have been able to judge of the correctness of our classification. The consensus of opinion of the nurse and teachers was that the children held close to their classification.

It is important to remember that the greater number of children with organic heart disease are of Class 1. It has been estimated recently[1] that 0.7 per cent. of every 100 school children in New York City have organic heart disease. Of that number 35 per cent. are Class 1, 37 per cent. Class 2, A, 7 per cent. Class 2, B, and 1 per cent. Class 3. The census of our clinic today shows that of 140 organic cases, 75 per cent. are Class 1; 16 per cent. are Class 2, A; 6 per cent. are Class 2, B, and 3 per cent. are Class 3. A comparison of the distribution of cases classified by clinical examination alone with that of those

classified by the aid of functional tests show a large percentage classified below actual tolerance, by the former method.


E. G. 12 years.
N.Y. NURSERY & CHILD'S HOSPITAL CARDIAC RESEARCH CLINIC.
DIAGNOSIS
M.R.S.
Class I
VITAL CAPACITY
c.c.
2400
2300
2200
2100
2000
1900
1800
1700
1600
1500
Jan 1920
Feb
Mar
Apr
May
June
July
Aug
Sept
Oct
Nov
Dec
Jan 1921
Feb
Mar
Apr
May
June
July
Aug
Sept
Oct
Nov
Dec
Jan 1922
Feb
Mar
Apr
May
June
July
Aug
Sept
Oct
Nov
Dec.
Jan 1923
Feb
Mar
Apr
May
June
July
Aug
Sept
Oct
Nov
Jan 1924
Pale – Cough
Nose Bleed
Ch. Arthritis – 4 days
Sick x 30
Sick x 30
Sick x 30

indicating the physical capacity of children with organic heart disease. A careful history and physical examination supplemented by these tests would seem to be the best practical method at present available for the classification and management of children with heart disease. The following cases will illustrate the practical and clinical value of these tests:

Case I.—E. G. first came to the Cardiac Clinic January, 1920, at twelve years of age. The past history was as follows: Occasional sore throats, frequent growing and joint pains and a mild arthritis. Cardiac involvement was of four years' duration. Tonsillectomy was refused. She was excused from school athletics and was restricted from free play, but admitted to taking part in all games equally well with her schoolmates. The clinic history from January, 1920 to January, 1924 is as follows: Except for an occasional sore throat and some joint pains and a mild rheumatic fever in April, 1922, she has been very well, the diagnosis being throughout this time mitral lesion, Class I. She has developed into a splendid girl in good physical condition. Graph of Case Record I is a true objective picture of her physical capacity and confirms the clinical history for the past four years.

Comment.—The persistent reduction of vital capacity of 10 to 13 per cent., notwithstanding a normal exercise tolerance for the seven test exercises, may be explained by the radiographic evidence of increased hilum shadow and thickened lung markings radiating to the periphery. These *x*-ray findings are, as a rule, associated with a reduction in vital capacity of 10 to 20 per cent. The gradual increase in vital capacity from 1980 to 2180 c.c. during four years is in accord with increased growth and development. It is of interest to note that the same percentage reduction from normal is still present.

Case II.—A. W., boy, ten and a half years of age, first came to the Cardiac Clinic in November, 1919, and has been under our care for the past four years. The past history consists of a mild sore throat and a severe chorea at five years of age, followed by cardiac involvement. The boy attended regular school and stated that he climbed five flights of stairs in his home equally well with his brothers. Physical examination showed a boy of poor nutrition and development, with enlarged tonsils and a mitral lesion. The vital capacity was minus 9 per cent. and he tolerated an average test exercise. He was classified as a Class I. subsequent history: The boy was admitted to a special segregated cardiac class. The accompanying graph of Case Record II shows that after four months the vital capacity increased to normal limits, and tonsillectomy was performed with no increased exercise in

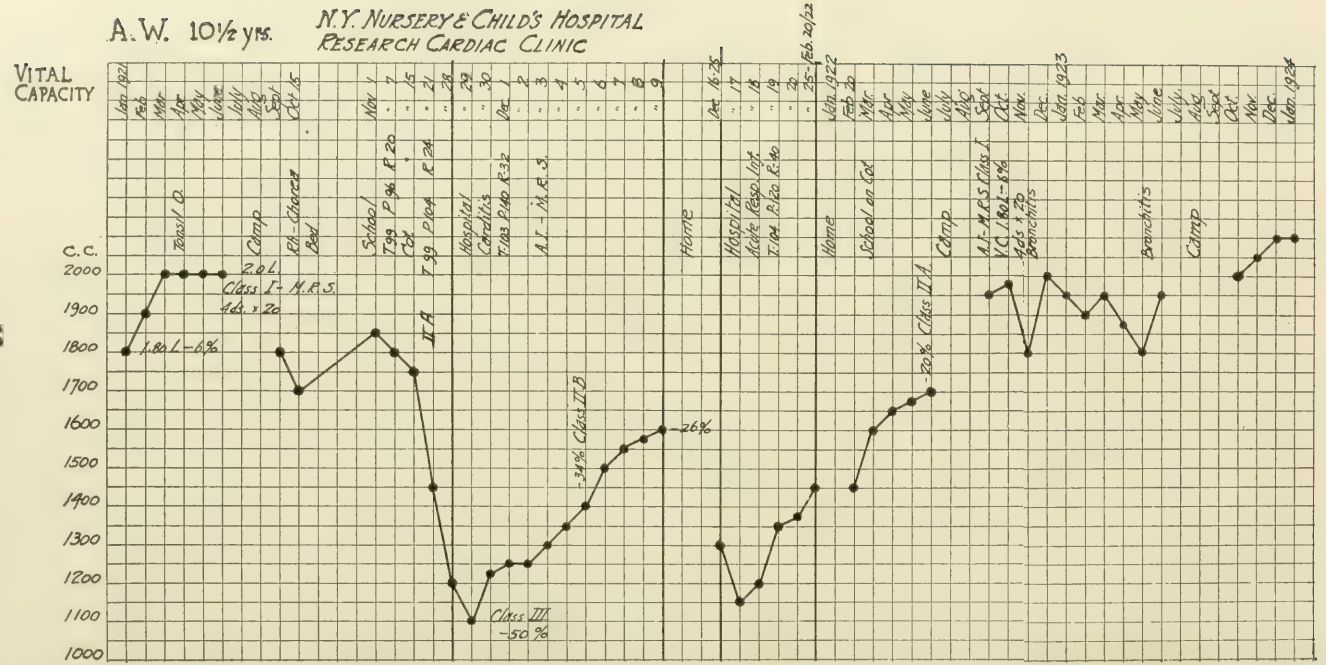


Fig. 47 (Case II).

July, 1921 he went to a Scouts' boys' camp which his brothers attended. While there he hiked, went swimming, and did not restrict his activities. He reported to the class September 15th in apparent excellent physical condition, stating that he felt perfectly well. Vital capacity record, however, showed a reduction in vital capacity, and he was advised to return to the special class for daily observation. October 15th he returned to the clinic for examination. He admitted some joint pains, and the school reported a change in disposition and a tendency to nervousness. The vital capacity showed a still further reduction. The boy was ordered to bed much against his wishes and returned to the clinic November 1st refusing to remain at home. The vital capacity showed a slight increase and he was allowed to return to school on a cot. The daily school record from November 1st to November 28th showed a pulse ranging from 85 to 100, temperature of 99° F., and some loss of weight. During these four weeks the boy rebelled against remaining on a cot and being carried upstairs to his home. The increasing reduction of his vital capacity was a true index of his clinical condition and prognosticated the acute carditis which ensued. He was admitted to the hospital ward on November 29th, with a diagnosis of acute carditis, aortic insufficiency, mitral stenosis, Class 3. While at the hospital daily vital capacity records showed a rapid increase in vital capacity for fourteen days, which was coincident with clinical improvement and the boy was taken home against advice, only to return in a week. His further progress was slow, and he was permitted to return to school on a cot when attaining a classification of 2, B. He refused to remain at home in bed. Eight months after his carditis he attained a classification of 2, A, and returned to camp in July, 1922, under restricted exercise. While there he gradually tolerated all but strenuous hikes and swimming. He returned to the clinic in September, 1922. At that time his vital capacity had reached normal limits and he was classed as a Class 1, and has retained this classification for the past two years.

Comment.—This case illustrates well the value of some objective test to determine physical capacity. This boy would never admit his incapacity, and were it not for the confirmative evidence afforded by these tests I do not believe we could have convinced his mother. The diminished vital capacity was important confirmatory evidence of the oncoming carditis and preceded the earliest clinical symptoms.

Case III.—C. V., girl, nine years of age, was first seen at the Cardiac Clinic on January 16, 1922. Her only complaints were loss of appetite and general malaise. The mother thought the child was well and tolerated exercise equally well with playmates. The past history revealed occasional sore throats, transient arthritis, and severe joint pains of three days' duration at six years of age. She was never known to have heart trouble. Physical examination showed a pale girl, underdeveloped, tonsils small and crypts loose clear, D'Espine

to the second dorsal, heart not enlarged, with a soft systolic murmur not transmitted. The vital capacity showed a reduction of 28 per cent. She was put to bed and returned a week later complaining of a persistent cough. The vital capacity was further reduced and she was classified as 2, B. A few days later she developed rheumatic

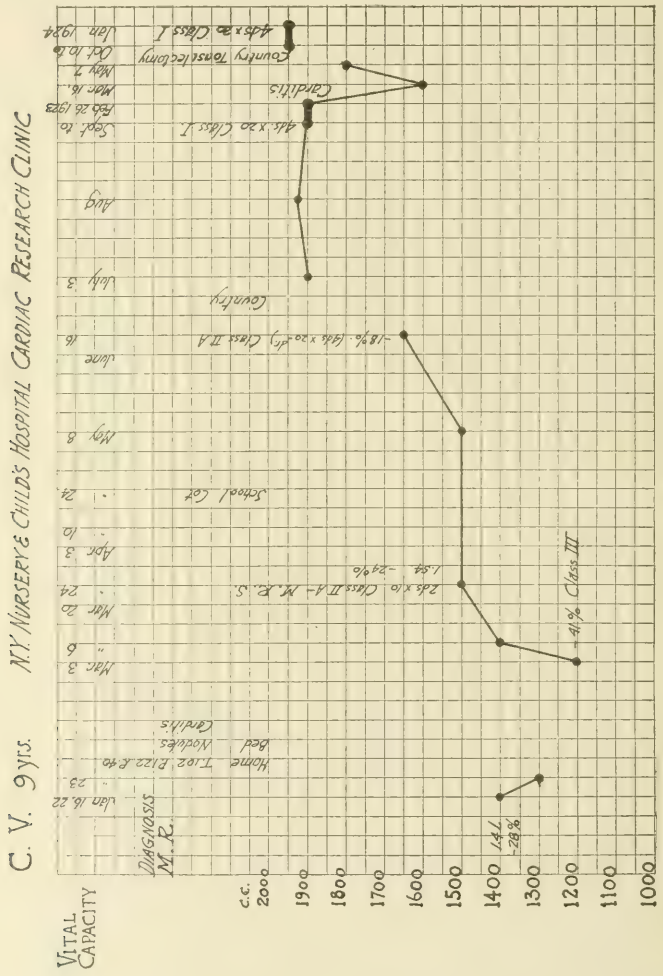


Fig. 48 (Case III).

nodules and a definite pericarditis. Graph of Case Record III shows the subsequent clinical course. After a severe illness of five weeks' duration the question of permitting the child out of bed was considered, but a vital capacity showing a reduction of 41 per cent. indicated the need of still further rest, although the parents and child claimed other-

wise, and the temperature had been normal for ten days and the pulse between 80 and 90. Three weeks later a vital capacity of minus 24 per cent. classified the case as 2, B, and the child was allowed out of bed. A month later she was permitted to attend school on a cot until a vacancy was available in a Convalescent Home. On June 16, three weeks later, the vital capacity was minus 18 per cent. In order to determine if this reduction in vital capacity was a true index of the exercise tolerance, an exercise test was given. She was unable to tolerate an average test exercise. After a month's stay at the Convalescent Home she returned to the clinic, and was found to have a vital capacity within normal limits and was able to tolerate an average test exercise. She was classified as Class 1, and retained this classification for seven months. In February, 1923, after an acute respiratory infection, she began to show some loss of weight. On March 10th her vital capacity showed a reduction and she was put in Class 2, A. A week later (April 18th) she developed a high temperature and a recurrent acute carditis with nodules. May 7th, following a week of normal temperature, the vital capacity showed an increase of 1800 c.c., a more rapid recovery than in her initial attack. After a tonsillectomy in June and a stay in a Convalescent Home she returned in the fall in splendid general condition, showing a vital capacity of 2100 c.c.

Comment.—This case again illustrates the value of functional tests in warning of the advent of a carditis before the clinical symptoms are sufficiently clear. This case also illustrates that the vital capacity may be used a factor in determining when a child may be permitted out of bed. This case also indicates every attack of carditis is not of equal severity or may not require the same period of convalescence.

Case IV.—[illegible] A. N., well-nourished boy, thirteen years of age, was referred to the Cardiac School April 9, 1921. He stated that he was perfectly well and able to compete with his school fellows and refused to enter the special class. His past history was as follows: Convalescence at six years of age, a chorea at ten years of age, and frequent growing and joint pains for the past year. His mitral lesion was found accidentally at nine years of age by a school physician. His vital capacity was 108 per cent., and he tolerated a severe test exercise. His diagnosis was mitral stenosis, Class 1. On September 11, 1921 he was sent for by the school nurse for follow-up. He did well to come to the clinic twice but he was very well. On examination he did not disclose symptoms of moment, but his vital capacity showed a reduction of 31 per cent. and he could not tolerate a severe test exercise, but was able to tolerate an average test exercise. Because of these findings he was refused to enter the special class and was put on a cot for observation. On September 18th he was allowed to school and remained there until December 19th, when he returned home for Christmas vacation. During the time at home he had some rheumatic pains, was put on cot, but refused to go to bed. On examination January 4, 1922 the [illegible]

was found to be pale, slightly dyspneic, the vital capacity showing a reduction of 51 per cent. He was classified as Class 3 and ordered to bed. Four days later he was seen at home acutely ill with a definite pericarditis. On January 23rd he was brought for examination to

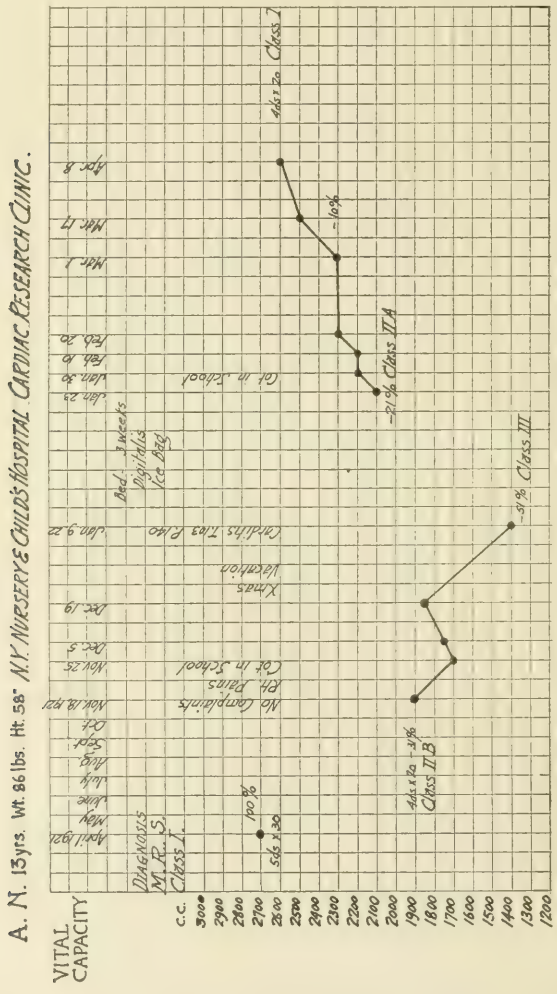


Fig. 49 (Case IV).

ascertain whether he could be permitted out of bed. Vital capacity showed a reduction of 21 per cent., and he was advised to go to a Convalescent Home, but he refused, and the mother urged us to admit him to school on a cot. Two months later he felt so well that he returned to a regular class in his previous school against advice, although his vital capacity had returned almost to normal.

Comment.—This case illustrates very well the value of having a previous record of vital capacity and exercise test, for not knowing the boy we would not have noted the significance of a vital capacity of 1900 c.c., since the reduction from the average would only have been about 20 per cent. Likewise, the fact that he was able to tolerate an average test exercise would have passed him as a Class 1 were it not for the fact that a previous record showed him able to tolerate a severe test exercise. It is important to remember the upper and lower possible normal limits. This boy is a typical example of the type that overestimates his ability and never gives in. He also illustrates the possible speedy recovery from a severe carditis which would ordinarily have indicated at least six weeks' rest in bed (which was ordered, but refused, apparently with no ill effects). This case must have had very little permanent involvement of the cardiac muscle.

Case V.—H. C., girl, ten years of age, was brought to the Clinic September 23, 1921, complaining of cough, dyspnea, and swelling of [illegible] duration. Her past history consisted of infrequent sore throats, chorea at four and six years of age, rheumatic fever at ten years of age. [illegible] For the past week she has not felt well and has had some joint pains. Physical examination showed a girl acutely ill, with apparent good general nutrition. [illegible] cyanosis and edema of the face, dyspneic, with respirations 40, and pulse 130. Throat was red, lungs congested, liver tender, heart enlarged, with a systolic and diastolic murmur. The vital capacity showed a reduction of 55 per cent., confirming the clinical diagnosis of cardiac failure. She was admitted to the ward and the accompanying graph, Case Record V indicates the clinical course. The daily increase of vital capacity was coincident with the rapid disappearance of symptoms. On October 12th tonsillectomy was performed, with an uneventful recovery, and the child was sent to a Convalescent Home. December 2nd she attained a vital capacity of minus 20 per cent., which is the highest that she has ever reached. Except for a relapse in six months she has been very well up to the present time. She has never reached a Class 1 classification.

Comment.—This case illustrates the use of the vital capacity as a possible therapeutic guide in the administration of digitalis. She is also an example of the type of case that probably never reaches a normal vital capacity.

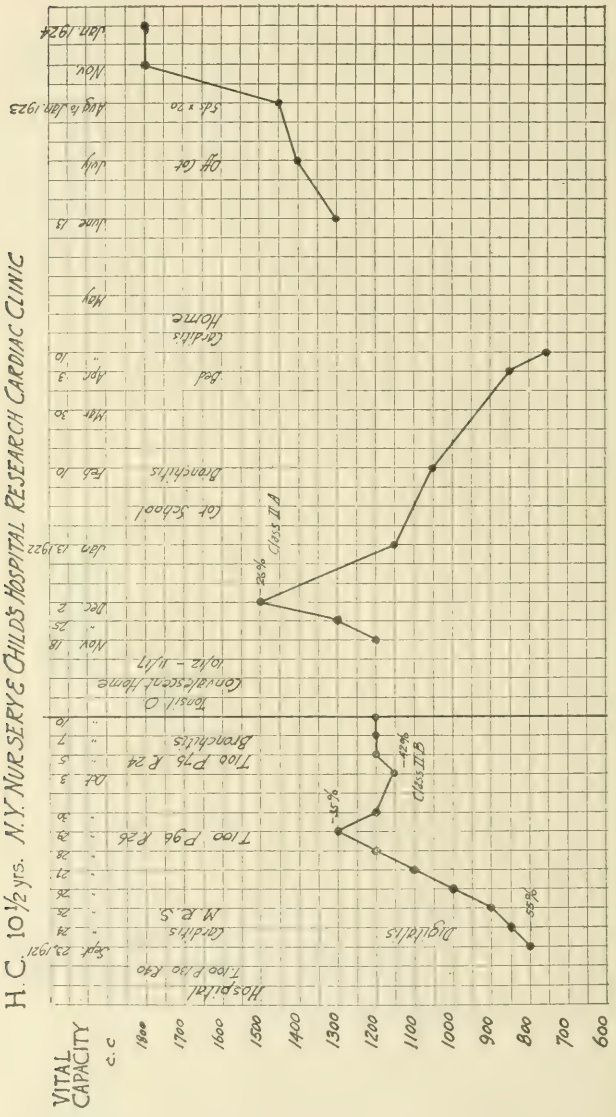


Fig. 50 (Case V).

Case VI.—M. M., girl, ten years of age, admitted to the ward February 4, 1921, with cough and high fever. Past history: Frequent recurrent attacks of bronchitis and sore throats with occasional joint pains. Cardiac condition was not known on admission. Physical examination revealed a well-developed girl acutely ill, with tonsils

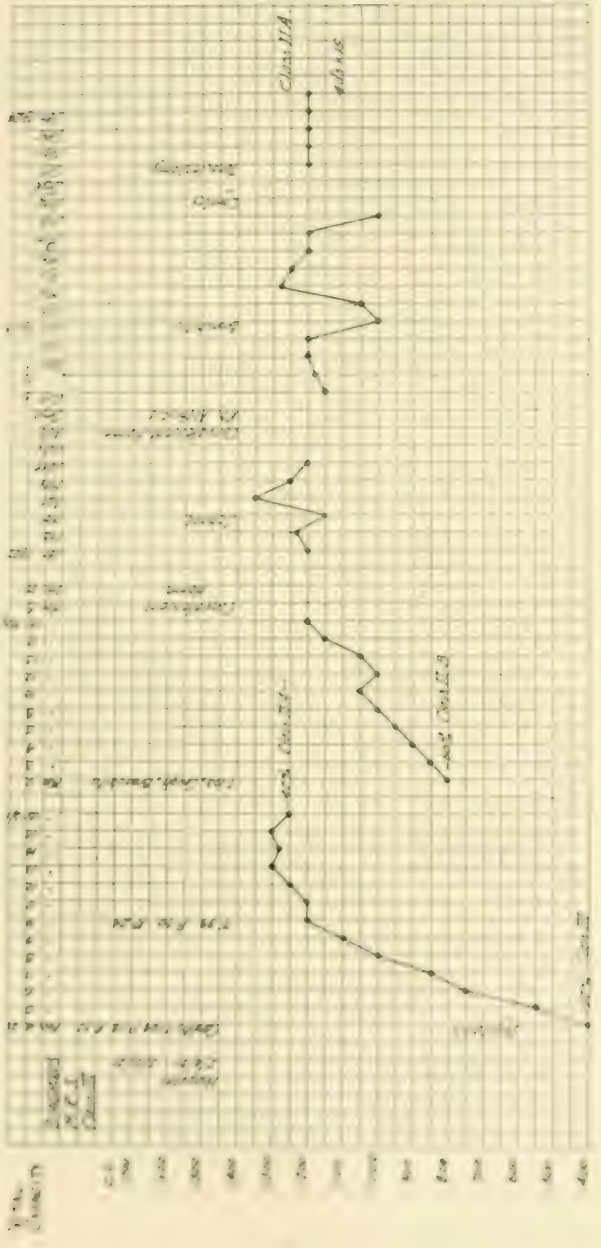


Fig. 51 (Case VI).

large and congested, lungs full of moist rales, liver tender, no edema, heart enlarged, with a systolic and diastolic murmur. Temperature 104° F., pulse 118, respirations 32. Vital capacity minus 82 per cent. The accompanying graph of Case Record VI of the vital capacity shows a rapid increase of vital capacity to about 50 per cent. in twelve days. On March 2nd, while still in the hospital in bed, a reinfection brought the vital capacity down to minus 60 per cent., with a return to previous level in two weeks, at which it remained for the ensuing two years.

Comment.—This case again illustrates the type of case that never becomes a Class 1. It is interesting to note that her best vital capacity is about minus 40 per cent. However, she was able to tolerate a mild test exercise, the increased reduction in vital capacity being due no doubt to the recurrent bronchitis.

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DEHYDRATION IN NEW-BORNS I*

HARRY EARWIN, M.D.
With the technical assistance of
CATHERINE GOSS, A.B.
NEW YORK

Since water is the medium in which the physical and chemical processes of the body take place, variations in the amount of the body fluids must be of great importance in the changes which occur during health and disease. The demonstration by Balcar and his associates [1] that fever may be produced by dehydrating animals makes the subject of particular interest in new-borns in whom fever and dehydration occur so frequently.

A number of observers believe that transient fever in the new-born is due to dehydration. This belief is based on the fact that the fever usually occurs at the time of the greatest weight loss in infants who have lost much weight. The loss of weight, it is assumed, indicates a water loss.

Objection has been raised to this conception of "inanition fever" [2] because many new-born babies lose considerable amounts of weight without developing fever while others develop fever after only slight losses of weight. In a subsequent paper we shall attempt to show that in the large majority of new-born babies with fever the plasma water is diminished. In this paper I propose to discuss the relation of weight loss to dehydration in new-born babies and to show the fallacy of drawing conclusions from the weight changes alone regarding the water content of the new-born.

The ease with which various tissues take up and lose water varies considerably. The muscles and skin apparently are very susceptible to changes in the water content of the organism. Tobler [3] dehydrated animals so that they lost from 25 to 30 per cent. of their body weight in a few days. He found that most of the water loss was accounted for by the loss in water from the muscles and skin. The blood and soft tissues lost comparatively little fluid. A number of observers [4]

* From the Pediatric Division of the New York Nursery and Child's Hospital and the Department of Pediatrics, Cornell University Medical College.

1. Balcar, J. O., Dawson, W. D., and Woodyatt, R. T.: Arch. Int. Med. **24**: 116 (Aug.) 1919.

2. Grulee, C. G., and Donar, B. E.: Am. J. Dis. Child. **22**: 44 (July) 1921.

3. Tobler, L.: Arch. f. exper. Path. u. Pharmakol. **62**: 431, 1909.

4. Engels: Arch. f. exper. Path. u. Pharmakol. **51**: 346, 1904. Rogers, L. J., Underhill, F. P., and Mendel, L. B.: Am. J. Physiol. **41**: 149, 419, 539, 1916. Smith, A. H., and Mendel, L. B.: Am. J. Physiol. **53**: 323, 1920.

have also shown that when saline is injected into the vein of an animal, the fluid quickly leaves the blood going for the most part to the muscles and skin thus increasing their water content. Recently Weed and McKibben [5] found that the water content of the brain is readily varied.

For a long time it was thought that, despite variations in the water content of the tissues, the blood water remained constant. It was believed that the tissues acted as a reservoir from which water might be withdrawn and to which water might be added without significantly altering the concentration of the blood. It is now known, however, that the blood water may change under a number of conditions.[6] Rogers, in 1909,[7] using the hematocrit, found that the blood may lose more than 60 per cent. of its water in cholera. Recently Underhill and his coworkers [8] showed that, accompanying the pulmonary edema seen in war gas poisoning and influenza, the blood may become concentrated. Numerous observations also show that in acute intestinal intoxication in infants the blood may become markedly concentrated.

When an organism loses water it does not lose it uniformly from all the organs. Certain organs (muscle, skin, brain) apparently give up water very readily, while others, such as the blood and soft tissues, remain comparatively unchanged until the water loss becomes marked. In some instances, however, fairly wide fluctuations may occur in the plasma water without corresponding changes in the water content of the baby.[9]

Fairly accurate methods are available for determining changes in the water percentage of the blood and plasma. Variations in the red cell content of the blood (also hemoglobin, dry residue of the blood, corpuscular volume, etc.) indicate changes in the percentage of water of whole blood. Variations in the plasma protein per cent. indicate changes in the plasma water per cent. The total plasma volume may also be determined. Since the red cell content of the blood during the first two weeks of life varies rapidly, due to causes other than changes in the blood water, determinations of the red cells, hemoglomin, etc., are of little value as indices of changes in the blood water content.

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5. Weed, F. S., and McKibben, L. H.: Am. J. Physiol. **48**:531, 1919.

6. Cushing, H., and Foley, F. E. B.: Proc. Soc. Exper. Biol. & Med. **17**: 1580, 1920.

7. Rogers, L.: Philippine J. Sc. **4**:99, 1909.

8. Underhill, F. P.: Arch. Int. Med. **23**:753 (June) 1919. Underhill, F. P., and Ringer, M.: J. A. M. A. **75**:1531 (Dec. 4) 1920.

9. For example, in a baby weighing 3,600 gm., 100 c.c. of saline by mouth reduced the serum protein per cent. from 7.55 to 5.93, indicating an increase of 27 per cent. in the plasma water. The amount of fluid given was only 3 per cent. of the body weight. In order to produce a corresponding increase in the water content of the rest of the tissues it would have been necessary to give nearly a liter of fluid.

In our experiments the refractive index of serum was used to measure changes in plasma water. Since, under most conditions, the plasma proteins are fairly constant, any change in their concentration is taken to indicate a change in the plasma water. The consistent results obtained in these experiments seem to indicate that in the newborn baby this assumption is, in the main, justified.

Method.—The serum protein percentage was determined with the Abbe refractometer. Distilled water was read with each series of readings. The factor for the nonproteins, determined in older infants [11] by the method of Robertson [11] was used. The calculation of the serum protein per cent. was made according to Reiss.[12]

The serum protein percentage is of importance not only because it measures changes in plasma water but also because it gives a measure of the osmotic resistance to the passage of water from the blood. The capillary wall acts as a semipermeable membrane [13] through which water and crystalloids (salts, sugar, urea, etc.) may pass freely but through which colloids are unable to pass. (In special situations, notably the liver, the plasma proteins are able to pass through the capillary wall, but in the main, Bayliss believes, the capillaries are impermeable to colloids). These colloids, the plasma proteins mainly, exert an osmotic pull on water which, according to Starling [14] amounts to from 30 to 35 mm. of mercury.

In the capillary we have, therefore, a force, the blood pressure, tending to squeeze water out of the circulation, while opposing it is the osmotic pressure of the plasma proteins which tends to hold water in the capillaries. One can readily understand that an increase in the plasma protein concentration, whether due to a diminution in the plasma water or to an actual increase in the plasma proteins, results in an increase in the resistance to the passage of water from the capillaries.

It is possible that the refractive index of the serum of the newborn baby gives only a rough estimate of the protein concentration of plasma. Lewis and Wells [15] have shown that in the serum of newborns euglobulin is almost entirely absent. The use of the factor 0.00372 (Reiss) for the calculation of the serum proteins is based on the assumption that the serum globulin and serum albumin exist in the same proportion as in the serum of adults. However, though the absolute values may not be correct, the relative differences of one

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10. Bakwin, H.: Am. J. Physiol. **60**: 343, 1922.
11. Robertson, T. B.: J. Biol. Chem. **22**: 233, 1915.
12. Reiss, E.: Ergebn. d. inn. Med. u. Kinderh., **10**: 311, 1912.
13. Bayliss, W. : J. Pharmacol. & Exper. Therap. **15**: 29, 1920.
14. Starling: J. Physiol. **19**: 312, 1896.
15. Lewis, J., and Wells, H. G.: U. S. M. A. **78**: 607 (March 25) 1922.

centration are sufficiently large so that the significance of the results is in no way diminished.

For purposes of comparison a chart showing the serum protein concentration of babies during the first week of life is shown(Fig. 1). Only afebrile babies are represented. It will be seen that the serum protein per cent. is usually between 6 and 7. It rises only rarely above 7.5, and in but three instances did it rise above 8. After the fourth day it is unusual to find the serum proteins above 7 per cent.

Hemoglobin was determined by the Palmer method.[16] The carbon monoxid standard was checked repeatedly with the Van Slyke and Stadie method [17] over a period of several months and found to check within 2 per cent. The hemoglobin results are charted in grams per hundred cubic centimeters of blood.

Fig. 1.—The serum protein per cent. of babies during the first week of life. The dots represent the individual determinations, the heavy black line the average serum protein per cent. Most of the points lie between 6 and 7 per cent., rarely above 7.5 per cent.

A loss of skin elasticity indicates that the water content of the skin is diminished below normal. In this discussion the degree of inelasticity has been designated by the number of pluses, 1 plus indicating a slight but distinct diminution in skin elasticity, 2 plus a more marked degree of inelasticity, etc.

THE RELATION BETWEEN CHANGES IN WEIGHT AND CHANGES IN THE WATER CONTENT OF THE NEW-BORN BABY

There are no direct methods for measuring variations in the water content of the tissues during life. The only indications of such changes are variations in the body weight and the condition of the skin. Freund [18] showed that the daily up and down curve of an infant's

16. Palmer, W. W.: J. Biol. Chem. **33**:119, 1918.
17. Van Slyke, D. D., and Stadie, W. J.: J. Biol. Chem. **49**:1, 1921.
18. Freund, W.: Jahrb. f. Kinderh. **59**:421, 1904.

weight is largely accounted for by changes in the water content of the organism. In the new-born a number of factors must be considered in estimating the significance of weight changes. The meconium, urine in the bladder, regurgitated allantoic fluid and vernix caseosa account for some of the weight loss. A part of it is also due to an actual loss of body tissue or stored food reserve during the starvation. This loss, according to Benedict and Talbot[19] amounts to about 17 gm. of fat per day for a baby weighing 3.76 kg. (from 35 to 40 gm. of protein or carbohydrate). The rest of the weight loss is due to water. For example, if a baby loses 300 gm. during the first three days of life, a not usually large loss, about 100 gm. are due to the loss of weight from meconium, etc.,[20] about 115 gm. at most, are due to loss of tissue

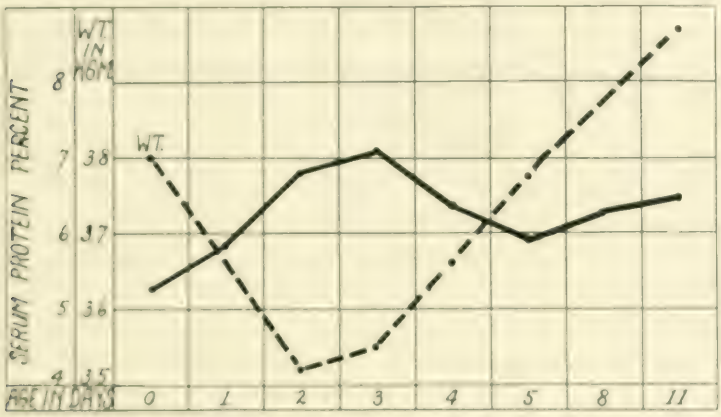

Fig. 2—Case 1. Increase in serum protein per cent. accompanying the loss of weight after birth. The serum proteins at birth were 5.23 per cent. Accompanying the loss of 280 gm. the serum proteins rose on the third day to 7.09. With the increase in weight between the third and fourth days the serum proteins fell to normal and remained there during the rest of the period of observation.

or food reserve and the remaining 85 gm. are due to water loss. Since most infants get some food during this time from the breast, and, at the New York Nursery and Child's Hospital, from whey which is given after each breast feeding, the water loss is probably considerably greater than the rough calculations just given indicate. It seems reasonable to assume, therefore, that the weight loss gives a rough index of the water loss in a new-born baby.

Variations in the Water Content of Babies at Birth.—In estimating the significance of weight changes in regard to the water content of the new-born baby at any particular time, it is essential that the water

19. Benedict, E., and Talbot, F.: Carnegie Institution Publication No. 231, 1915, p. 11.

20. Vierordt-Gerhardt: Handbuch der Kinderkrankheiten, 1:448, 1877; quoted by Griffith: Diseases of Children, Philadelphia, 1:46, 1921.

content of the baby at birth be considered. For example, a baby who has a large water reserve at birth can lose a great deal more weight without becoming dehydrated than can another infant who is dehydrated at birth.

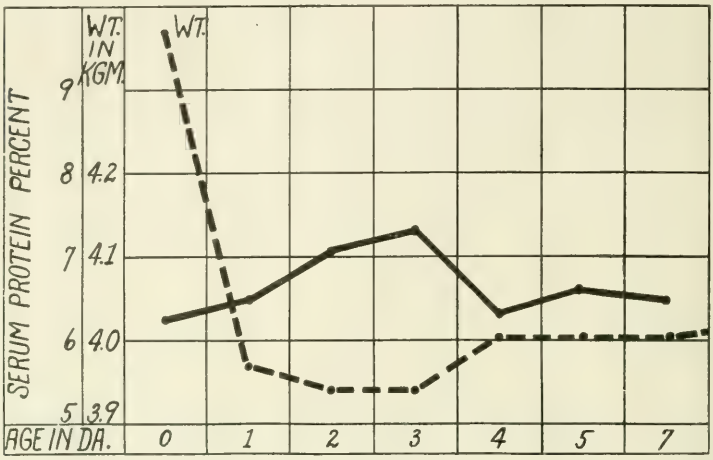

Fig. 3.—Case 2. Increase in the serum proteins accompanying the loss of weight after birth. In this baby the loss of 430 gm. was accompanied by a rise of the serum proteins from 6.28 to 7.31 per cent. With the increase in weight the serum protein concentration dropped to normal and remained there.

TABLE 1.—Dehydration Accompanying the Loss of Weight After Birth

Case	Age, Days	Weight, Gm.	Serum Protein, %	Hemoglobin, Gm. per 100 C.c.	Skin
1	Birth	3,800	5.23	....	Normal
(Fig. 2)	1	.....	5.87	....	1 plus, inelastic
	2	3,520	6.80	....	1 plus, inelastic
	3	3,520	7.09	....	1 plus, inelastic
	4	3,660	6.34	....	Normal
	5	3,750	5.93	....	Normal
	8	.....	6.28	....	Normal
	11	3,970	6.45	....	Normal
2	Birth	4,370	6.28	18.3	Normal
(Fig. 3)	1	3,970	6.51	17.8	1 plus, inelastic
	2	3,940	7.09	19.2	1 plus, inelastic
	3	3,940	7.31	17.2	1 plus, inelastic; Temp. in a.m. 38 C.
	4	4.040	6.34		
	5	4,010	6.62	20.3	Normal
	7	4,040	6.45	....	Normal

The case reports show that the water content of the baby at birth may vary widely. Usually, as the baby loses weight during the first few days after birth, the skin becomes inelastic and the plasma concentration increases indicating a diminution in skin and plasma water (Table 1).

Two babies (Cases 1 and 2) showed no evidence of dehydration at birth. The skin turgor was good and the plasma concentration

(serum protein per cent.) not increased. During the first three days of life they lost considerable amounts of weight. The weight loss was accompanied by an increase in the plasma concentration and a loss of skin elasticity (diminution of plasma and skin water). As the babies started to gain the blood and skin returned to normal.

An increase in the serum protein concentration during the loss of weight after birth has been noted by Rott[21] and by Rusz.[22] The hemoglobin per cent. in Case 2 varied from day to day without relation to weight or serum protein per cent.

There are babies, however, who apparently are born with a large water reserve. In these babies the weight loss is unaccompanied by any detectable evidence of dehydration (Table 2). Such cases have been described by Utheim[23] Two babies (Cases 3 and 4) lost considerable amounts of weight without showing any evidence of skin or

TABLE 2.—Loss of Weight Unaccompanied by Dehydration

Case	Age, Days	Weight, Gm.	Serum Protein, %	Hemoglobin, Gm. per 100 C.c.	Skin
3	Birth	3,170	6.57	[illegible]	Normal
	1	3,080	6.70	19.8	Normal
	2	3,040	6.78	20.3	Normal
	3	2,830	5.75	[illegible]	Edema of dorsum of hand and foot
	4	2,810	[illegible]	19.9	Normal
	5	2,770	5.40	19.2	Normal
	6	2,840	5.87	[illegible]	Normal
4	Birth	3,860			
	1	3,760	6.24	[illegible]	Normal
	2	3,580	6.68	[illegible]	Normal
	3	3,580	6.23	[illegible]	Normal
	5	3,500	5.94	[illegible]	Normal
	7	3,600	6.16	[illegible]	Normal
	11	3,800	6.11	[illegible]	Normal

plasma dehydration. It is possible that the water reserve was large at birth, or that the water lost came from the deeper tissues such as the muscles, etc., where it could not be detected by the methods employed. It is possible that the weight loss was accompanied by a destruction of the plasma proteins so that a diminution in the plasma water might have occurred which was compensated for by a loss of plasma protein. The fact that the skin as well as the plasma did not become dehydrated, despite the weight loss, seems to indicate that the water reserve in these babies was large at the start. Whatever the explanation for the failure of the plasma to become concentrated, however, the fact remains that, in spite of the loss of considerable amounts of weight in certain babies, the serum protein concentration remains normal. This is of considerable importance in view of the close rela-

21. Rott, F.: Pirquet's Handb. f. Kinderh. (Originalbeit.) **1**: 43, 1910.
22. Rusz, E.: Monatsschr. f. Kinderh. (Originalien) **10**: 580, 1912.
23. Utheim, K.: Særtrykk av Norsk Mag. f. Lægevidensk., 1921, p. 104.

tionship between fever in the new-born and an increase in the serum concentration.

In the two cases just described the weight loss was unaccompanied by any evidence of dehydration, probably because the babies had large water reserves at birth. There are babies, however, who are dehydrated at birth. In one of the babies referred to the skin alone was involved; in

TABLE 3.—Skin Dehydration at Birth

Case	Age, Days	Weight, Gm.	Serum Protein, %	Hemoglobin, Gm. per 100 C.c.	Skin
5	Birth	3,750			
	1	3,750	6.16	19.2	2 plus, inelastic, dry
	2	3,490	7.14	22.1	2 plus, inelastic, dry
	3	.....	....	20.7	2 plus, inelastic, dry
	4	3,440	7.31	20.3	2 plus, inelastic, dry
	5	3,490	6.63	21.0	2 plus, inelastic, dry
	6	3,550	6.28	21.3	2 plus, inelastic, dry
	8	3,580	6.86	19.6	Doubtful
	12	3,600	6.57	....	Normal

the two others, the skin and plasma. Case 5 was first observed fifteen hours after birth (first day). At this time the skin was dry and inelastic, indicating a diminution in skin water. The plasma water was normal. As the baby lost weight the plasma quickly became concentrated. With the increase in weight on the fifth day the plasma returned to normal. The skin, however, remained dehydrated for several days afterward. Case 6 was observed three hours after birth;

TABLE 4.—Skin and Plasma Dehydration at Birth

Case	Age, Days	Weight, Gm.	Serum Protein, %	Skin
6	Birth	2,950	7.43	3 plus, inelastic, dry
	1	2,890	7.61	3 plus, inelastic, dry
	2	.....	8.02	3 plus, inelastic, dry
	3	2,890	6.91	3 plus, inelastic, dry
	4	3,010	6.97	3 plus, inelastic, dry
	6	3,130	6.61	Normal
	12	3,290	6.51	Normal
7	Birth	3,320		
	1	3,290	7.48	3 plus, inelastic, dry
	2	3,290	8.06	2 plus, inelastic, dry
	3	3,140	7.48	2 plus, inelastic, dry
	4	3,140	7.20	3 plus, inelastic, dry
	6	3,260	7.55	Dry, no loss of elasticity
	8	3,320	6.74	Normal

another baby (Case 7) was seen thirteen hours after birth. During this time the latter had lost 30 gm., an insignificant loss in weight and hardly sufficient to account for the dehydration. At the first observation both showed distinct evidence of skin and plasma dehydration as indicated by the marked skin inelasticity and the high serum protein concentration. At this time they were more dehydrated than most of the afebrile babies who had lost large amounts of weight.

The desiccation persisted as long as the babies continued to lose weight. In Case 6 the serum protein concentration returned to normal two days before the skin. In Case 7 the skin regained its elasticity before the plasma water had returned to normal.

At birth, apparently, the water content of the baby may show many degrees of variation. At one extreme is the watery baby who may lose considerable amounts of weight without showing any evidence of dehydration. At the other extreme is the dried out, desiccated baby who at birth shows a dry, inelastic skin and a concentrated plasma. Between these two extremes all gradations exist.

Increase in the Plasma Water Without Increase in Weight.—Another point to be considered in estimating the significance of weight changes in regard to the water content of the baby is the transportation

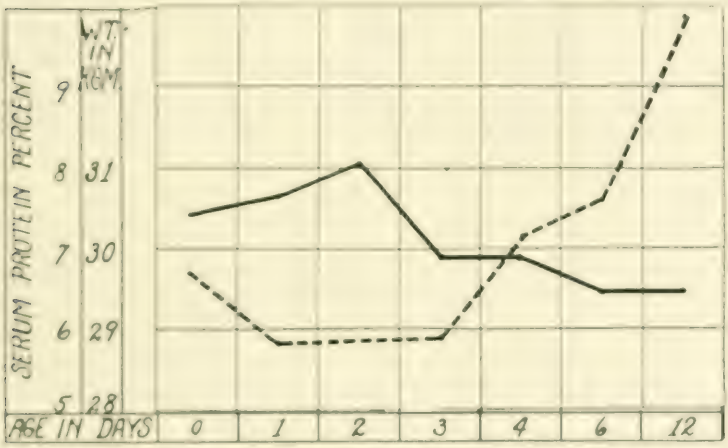

Fig. 4.—Case 6. Dehydration at birth. On the birthday the serum protein per cent. was 7.42 per cent., indicating a concentrated plasma. A loss of a few grams was accompanied by a rise of the serum proteins to 8.02 per cent., a high figure rarely reached by afebrile babies. Between the third and fourth days the serum proteins fell to 6.92 and remained normal thereafter.

of water in the baby from one tissue to another. In a few instances we have noted a fall in the serum protein concentration from one day to another without any increase in weight.

In two babies (Cases 8 and 9) the plasma became more watery despite the fact that the weight did not increase. The decrease in the plasma concentration may have been due to an increase in plasma water or to a destruction of plasma proteins. Whatever the explanation, however, the fact remains that an increase in the plasma water per cent. may occur without any increase in weight.

The Relation Between Skin and Plasma Water in the New-Born.—When dehydration develops in a new-born baby it is usual for the skin

to lose its elasticity before the plasma has become concentrated and to persist for some time after the plasma water has returned to normal (Cases 1, 2, 5 and 6). It is not at all unusual to find the skin inelastic in a baby whose plasma is normal or even dilute (Case 1, second day). Marked degrees of skin inelasticity are usually accompanied by an increase in the plasma concentration although this is by no means always the rule (Case 6).

TABLE 5.—Increase in Plasma Water Without Change of Weight

Case	Age, Days	Weight, Gm.	Serum Protein, %	Hemoglobin, Gm. per 100 C.c.	Skin
8	Birth	3,260			
	1				
	2	3,180			
	3	3,120	....	7.3	1 plus, inelastic
	4	3,120	8.49	15.9	1 plus, inelastic
	5	3,120	6.91		
	6	3,120	6.57	15.6	Normal
	7	3,120	6.57	....	Normal
9	Birth	3,690			
	1	3,690	8.49	....	1 plus, inelastic, dry
	2	3,630	7.31	....	2 plus, inelastic, dry
	3	3,630			
	4	3,690			
	5	3,750			

An increase in the plasma concentration is usually accompanied by a loss of skin elasticity. In a few instances the skin was normal while the plasma was concentrated (Case 7, sixth day). In one baby with a serum protein per cent. of 9.40, the skin, although very loose, showed no evidence of dehydration. In the fever cases, particularly, the plasma may be markedly dehydrated with only slight impairment of the skin elasticity.

The Relation Between Hemoglobin Per Cent. and the Water Content of the New-Born Baby.—In a number of cases, daily determinations of the hemoglobin were made. No relation, however, was found between the weight changes, serum protein percentage and the hemoglobin.

SUMMARY AND CONCLUSIONS

1. Dehydration was studied in new-born babies by correlating weight changes, skin elasticity and serum protein concentration (plasma water).

2. Uusually a marked weight loss in the new-born baby is accompanied by a loss of skin elasticity and an increase in the serum concentration (indicating a diminution in skin and plasma water).

3. There are babies, however, who, despite relatively large weight losses, show no evidence of dehydration of the skin or plasma In these babies, presumably, the water reserve of the tissues at birth is large.

4. On the other hand, there are babies who show evidence of dehydration at birth. The skin alone may be desiccated (loss of skin elasticity without increase in the serum protein concentration) or both skin and plasma may be involved (loss of skin elasticity and increase in serum protein concentration).

5. Since the water content of the baby varies so widely at birth it is impossible to tell from the weight curve alone whether or not a baby is dehydrated.

6. The plasma water per cent. may increase even though there is no increase in weight.

7. Impairment of skin elasticity may, and often does, occur without increase in the plasma concentration. Increase in the plasma concentration is usually, but not always, accompanied by an inelastic skin.

It is with pleasure that I acknowledge my indebtedness to Dr. H. M. Painter and Dr. Fellows Davis, Jr., for the use of material from the Obstetrical Service of the New York Nursery and Child's Hospital. I wish to thank Dr. J. F. Sammis and Dr. L. C. Schroeder for their stimulating interest in the work. Thanks are due to Dr. Donald McGill, Resident, for his cooperation and to Miss Ethel Viele for her valuable assistance.

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DEHYDRATION FEVER IN NEW-BORNS II*

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With the technical assistance of
CATHERINE GOSS, A.B.
NEW YORK

The frequent occurrence of a transient fever during the first few days of life is now generally recognized. The exact nature of the fever has not yet been satisfactorily explained. Holt,[1] who gave the first adequate description of the condition in 1895 ascribed it to starvation and called it inanition fever.

Of the many hypotheses which have been advanced to explain this peculiar fever the one which has received the most experimental support is that which attempts to explain the fever as due to water loss. The observation originally made by Holt that the fever usually occurs at the time when the weight loss is greatest and disappears when the baby starts to gain has been amply confirmed.[2] Holt also showed that the fever can be made to disappear by administering fluids.[3] He mentions instances of fever in older infants on low fluid intakes which cleared up when fluid was given. Stewart[4] succeeded in reducing the incidence of fever in new-borns by giving lactose solutions between nursings. Faber[5] practically prevented fever in new-borns by complemental feedings of whole milk dilutions.

In 1910, Erich Mueller[6] described two cases of fever in older infants who were receiving very little fluid. In both instances the temperature fell to normal when fluids were given. Grulee and Bomar[7] described similar instances of fever in infants who were receiving concentrated diets. In these babies, as in Mueller's, the fever disappeared when fluids were given. In one of their babies the red cell content of the blood was high during the fever falling after the temperature had become normal. They interpreted the high red cell count as indicating a diminution in the blood water. Marriott[8] has suggested that the fever which occurs so frequently in babies with severe diarrhea may be due to dehydration.

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2. Von Bonar, A. B.: Zeschr. f. Kinderh. (Originalien) **4**: 37, 1912. Heller, F.: Zeschr. f. Kinderh. (Originalien) **4**: 55, 1912.
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4. Stewart, C. A.: J. A. M. A. **78**: 1864 (June 17) 1922.
5. Faber, H. K.: Am. J. Dis. Child. **24**: 56 (July) 1922.
6. Mueller, E.: Berl. klin. Wchnschr. **47**: 673, 1910.
7. Grulee, C. G., and Bomar, B. E.: Am. J. Dis. Child. **21**: 220 (March) 1921.
8. Marriott, W. M.: Harvey Lectures, 1930.

In 1915, Balcar, Sansum and Woodyatt [9] produced marked degrees of fever in animals by severely dehydrating them with intravenous injections of hypertonic glucose solutions given rapidly. They suggested that the fever was due to a failure of normal heat loss because of lack of water evaporation from the body.

Barbour and Howard [10] showed that the fall in temperature following the administration of glucose to dogs with fever is accompanied by a hemodilution (decrease in the hemoglobin per cent. of the blood). They also found that in colon bacillus fever in animals and in human febrile cases antipyrin, quinin and salicylates reduce the blood concentration. Schmitt and Sansum [11] succeeded in reducing the temperature of patients with pneumonia and influenza several degrees and in some instances below 37.8 C. (100 F.) by giving large quantities of fluid by mouth. In a recent review Barbour [12] strongly favors the view that "body temperature is regulated by water shifting under nervous control."

The investigations described in this paper were undertaken in an attempt to determine the relationship between dehydration and fever in the new-born. Three methods were used for estimating dehydration, the plasma concentration (refractive index of serum), the condition of the skin and the weight loss.

The applicability of these methods to a study of dehydration in the new-born has been discussed in the previous paper.[13] It was pointed out that the water content of babies at birth varies widely. Usually a distinct weight loss during the first days after birth is accompanied by a loss of skin elasticity and an increase in the plasma concentration indicating a loss of water from the skin and plasma. In some babies, however, comparatively large weight losses occur without the development of skin or plasma dehydration. In these babies, presumably, the water reserve at birth is large. On the other hand, some babies at birth show evidence of skin and plasma dehydration (loss of skin elasticity and increase in serum protein concentration). From the weight curve alone, therefore, one cannot draw conclusions as to the water content of the new-born baby; the water content of the baby at birth must also be considered. This variation in the water content of the baby at birth explains the occurrence of dehydration fever in new-borns without very large weight losses (dehydration at birth).

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It also explains the lack of fever in certain babies who lose a great deal of weight (large water content at birth).

Procedure and Methods.—Daily determinations were made on a group of normal and febrile babies. Blood for refractive index (and in a number of cases for hemoglobin) was drawn from the toe without pressure from three to four hours after a feeding. The temperature of the baby was taken at the time of the puncture. Details of the technic for the serum protein (refractive index of serum) and hemoglobin determinations are given elsewhere.[13]

The only study recorded in the literature on the plasma water in new-born babies with fever is that of Utheim.[14] She concluded that fever in the new-born may occur without a simultaneous increase in the concentration of the plasma. The refractometric method was used.

According to Reiss[15] in older infants with fever due to various infections, the plasma is more dilute than normal (refractometric determination of serum). A large number of determinations made in this laboratory during the past three years showed no increase in the serum protein concentration during the fever associated with various infections. We have had little opportunity to study the plasma concentration in new-borns with fever due to infections. In one baby 5 days old with sepsis and a temperature of 40.6 C. (105 F.) the serum protein was low—5.67 per cent. In another new-born baby with diarrhea and a temperature of 38.3 C. (101 F.) the serum protein was 6 per cent., which is a low normal.

Observations were made on fifty new-borns with fever. Of these, one case each of sepsis, diarrhea and hemorrhagic disease have not been used in the preparation of Figure 1. In these cases the serum protein concentration was not increased. The remaining forty-seven cases with which this paper concerns itself conformed fairly closely to the classical description of inanition fever. The fever usually occurred from forty-eight to ninety-six hours after birth in babies who had lost considerable amounts of weight. In some of the babies, however, the onset of the fever was within the first thirty-six hours after birth and in some the weight loss was not marked.

The skin usually showed some evidence of dehydration (dry, inelastic skin). In most instances this was not more marked than in the afebrile babies. The association between fever in new-borns and a loss of skin elasticity is not a close one. Some of the babies, particularly those with a high serum concentration, appeared to be quite ill. They were prostrated, apathetic, limp and at times looked gaily. Other babies, however, with equally high serum concentrations did not appear ill.

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In Figure 1 are shown the results of serum protein determinations on normal and febrile babies. The dots represent the afebrile babies, the crosses the febrile. The lower line represents the average normal serum protein percentages each day; the upper line the average for the febrile babies. The serum protein per cent. of normal new-borns lies fairly constantly between 6 and 7. In only three of the babies did it rise above 8 per cent. In the febrile babies the serum protein was usually above 7.5 per cent. In five babies it rose above 9 per cent., as high a figure as is seen in many severe cases of acute intestinal intoxication in older infants. These results show that in the group of cases of fever studied the plasma concentration was definitely increased.

In eight babies the serum proteins did not rise above 7 per cent. during the fever. In five of these the fever was associated with a

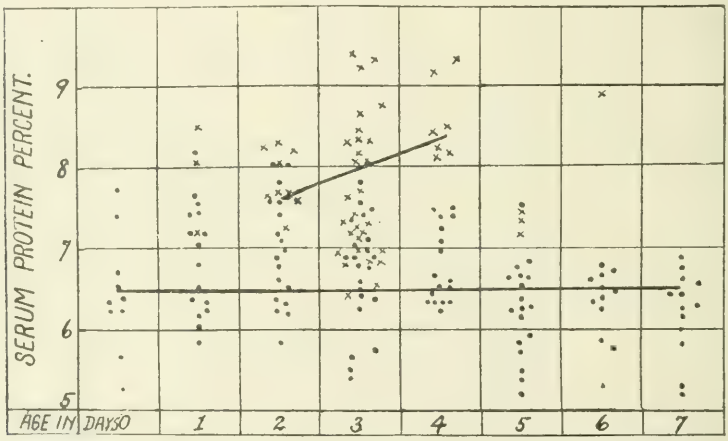

Fig. 1.—The serum protein per cent. in dehydration fever in new-borns. Dots, normal babies; crosses, febrile babies. Upper black line, average for febrile babies; lower black line, average for normal babies.

febrile affection in the mother. It seems possible that a pyrogenetic substance may be transmitted from mother to baby in these cases (Cases 7 and 8). In Case 8 mother and baby had fever at varying times for twenty-seven days after the delivery (Fig. 8). There is fairly close parallelism between rises in the temperature of the mother and baby. The baby's serum protein concentration on the second day of life, when the temperature was 40.7 C. (105.2 F.) was 6.97 per cent., which is within normal limits. In Case 7 the temperature of the mother rose at the same time as the baby's. The baby's temperature remained elevated until it was weaned on the sixth day. In this case also, the serum proteins were not increased.

In Table 1 are shown the weight losses and the serum protein percentages (plasma concentration) of a group of normal and febrile babies. The weight losses in babies with dehydration fever vary from 60 to 700 gm., averaging 350 gm. In the normal babies the weight losses varied from 120 to 540 gm., averaging 280 gm. It will be seen that fever, though more common in babies who had lost a great deal of weight, nevertheless occurred in babies who had lost only small amounts. In these latter babies, however, the increase in serum concentration was as marked as in babies who had lost larger amounts of

TABLE 1—THE WEIGHT LOSS AND THE SERUM PROTEIN PERCENTAGE IN NORMAL AND FEBRILE BABIES

Normal Babies		Febrile Babies	
Weight Loss, Gm.	Serum Protein, per Cent.	Weight Loss, Gm.	Serum Protein, per Cent.
		[illegible]	9.40
		[illegible]	8.96
		[illegible]	8.77
		[illegible]	8.49
		[illegible]	7.88
360	7.40	[illegible]	8.20
		540	8.61
60	6.97	480	[illegible]
420	7.31	420	8.89
420	[illegible]	420	8.02
420	7.25		
360	6.18	300	8.24
300	[illegible]	300	[illegible]
300	7.31	300	8.73
300	[illegible]	300	7.14
240	6.53	300	7.26
		480	8.89
		300	7.26
240	[illegible]	300	9.29
240	7.81		
240	[illegible]		
360	6.86		
300	[illegible]		
180	[illegible]	180	7.31
180	[illegible]	180	[illegible]
180	7.45	150	8.49
180	6.29		
180	[illegible]		
120	6.69		
		90	8.37
		60	8.43

weight. Losses of weight, therefore, are of significance in relation to fever in the new-born only as they affect the plasma concentration. Since the water content of the baby varies so widely at birth, the weight loss, except perhaps when marked, gives but a poor index of the water content of the plasma.

The hemoglobin varied from day to day without relation to fever, weight or changes in the serum protein per cent. Though there is no relation between variations in the hemoglobin and fever, it is possible that the high red cell content of the blood of new-born babies, by increasing the blood viscosity and thereby slowing the peripheral blood flow, might tend to diminish heat loss and hence make the occurrence of fever more likely.

Comment.—During recent years a considerable amount of evidence has accumulated showing that a close relationship exists between fever and water shifting. In our studies on fever in the new-born, a large proportion of the cases showed a well marked increase in the serum protein per cent., indicating a diminution in plasma water. The concentration of the serum proteins was often as marked as is seen in infants with acute intestinal intoxication. The drop in temperature was accompanied by a well marked drop in the serum concentration. Though the serum of afebrile babies also became concentrated during the loss of weight which occurs in the first three or four days of life, this was rarely as marked as in the febrile babies. Similar increases in the serum concentration are not found in babies with fever due to various infections. It seems clear, therefore, that the cases of fever in new-borns differ from the fevers due to infections in that they are associated with a diminution in the plasma water.

Confirmatory evidence of the close relationship between dehydration and these cases of fever is found in the readiness with which the fever can be reduced by giving fluids. In a number of instances water or glucose solution, warmed to a temperature above that of the baby, was given by gavage. In the large majority of cases so treated the temperature fell several degrees in from thirty to sixty minutes after the gavage.

It seems probable that other factors contribute to the ease with which new-born babies develop fever. It is not unlikely that the high red cell content of the blood, by increasing the viscosity, slows the rate of blood flow and thus diminishes heat elimination.

In the two cases mentioned infections in the nursing mother were associated with fever in the baby. In these babies the serum protein concentration was not increased. It is conceivable that minor disturbances in the mother which pass undetected may also be factors in predisposing, or in some instances causing, fever in the new-born baby.

SUMMARY OF CONCLUSIONS

1. A group of cases has been described in which fever in the new-born baby was associated with a diminution in the plasma water (increase in the serum protein concentration). The fall in temperature was coincident with an increase in the plasma water.

2. A similar increase in the serum concentration is not found in normal new-borns nor in babies in whom fever is due to other causes.

REPORT OF CASES

The following case reports illustrate the close relationship between fever in the new-born baby and the plasma water. Two cases in which fever in the baby was associated with fever in the mother are also shown.

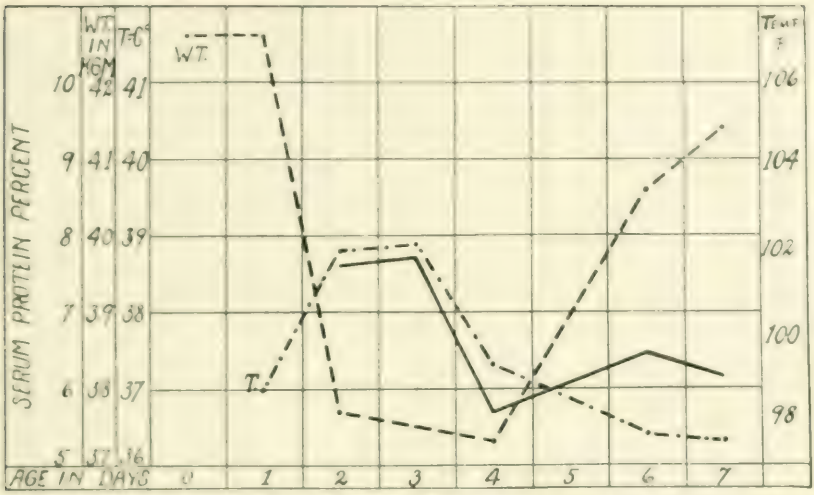

Fig. 2 (Case 1).—The relation between temperature, weight loss and serum protein per cent. (plasma concentration) in dehydration fever. The loss of weight is accompanied by a rise of temperature and an increase in the serum protein per cent. The temperature and serum protein per cent. fall on the fourth day and remain normal thereafter.

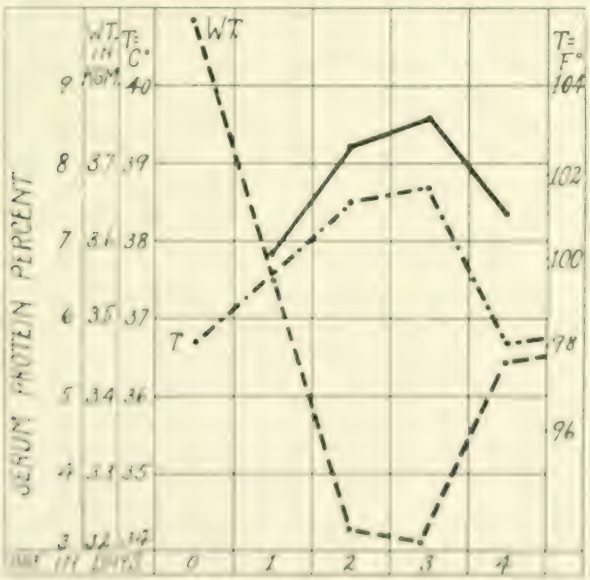

Fig. 3 (Case 2).—The relation between temperature, weight loss and serum protein per cent. (plasma concentration) in dehydration fever. In this case a marked loss in weight is accompanied by a rise of temperature and an increase in the serum protein per cent. The temperature and increased serum concentration persist until the weight again starts on the fourth day, after which they are normal.

Case 1 (Fig. 2).—*Dehydration Fever.*—The mother was a primipara, aged 26. Labor was normal. On the afternoon of the delivery the temperature rose to 38.5 C. (101.2 F), but after this it was normal.

At birth the baby weighed 4,260 gm. and was apparently vigorous. During the first two days after birth he lost 490 gm. The temperature, which up to that time had been normal, rose to 38.8 C. (101.8 F.). The patient seemed well otherwise, except that the skin was 2 plus inelastic. The serum protein concentration was 7.61 per cent., indicating a diminution in the plasma water. The fever and hehydration (loss of skin elasticity and increased serum protein concentration) persisted on the third day. On the fourth day, the temperature fell to normal, and at the same time the serum protein per cent. dropped from 7.70 to 5.70 per cent. The baby continued to gain well after this, and the serum protein per cent. remainded normal during the rest of the period of observation.

Case 2 (Fig. 3).—*Dehydration Fever. Reduction in Temperature and Serum Concentration Following the Administration of Fluids.*—The mother was a primipara, aged 24. The delivery and postpartum course were normal without fever.

The baby weighed 3,880 gm. at birth and seemed to be vigorous. When first observed, twenty-three hours after birth, he had lost 280 gm. The temperature was normal, and there was no evidence of skin or plasma dehydration. The baby continued to lose weight, and by the second day had lost a total of 540 gm. On this day his temperature rose to 38.5 C. (101.4 F.). The skin was slightly inelastic (1 plus), and the serum proteins had risen from 6.86 on the first day to 8.20 on the second. The fever persisted on the third day, the skin and plasma remaining dehydrated. Between the second and third days there was a further loss of 80 gm.

During the night following the third day the patient was given an ounce of 5 per cent. glucose solution, every two hours, in addition to the regular breast feeding. On the fourth day his weight had increased 230 gm. The temperature was normal, and the serum protein per cent. dropped from 8.60 on the third day to 7.31 on the fourth day. The baby continued normally after the fourth day.

Case 3 (Fig. 4).—*Dehydration Fever Occurring Within Thirteen Hours After Birth.*—This was the mother's second pregnancy. The first child, a girl, was 3 years old and quite well. The postpartum course was normal except for fever and pain in the lower abdomen on the fourth day postpartum.

The patient weighed 3,800 gm. at birth. He was first seen thirteen hours after birth. He had lost 190 gm., the skin was slightly inelastic (1 plus), and the temperature, which was normal at the time of birth, had risen to 38.7 C. (101.8 F.). On the next day the temperature had risen still further, to 40.2 C. (104.2 F.), and the patient had lost an additional 150 gm. By the next day (third day) the baby had gained 90 gm., the temperature had fallen to normal, and he continued afebrile after this. During the fever the serum protein per cent. was increased, falling on the third day with the subsidence of the fever. The baby's temperature rose and fell before the mother's indisposition on the fourth day.

Case 4.—*Dehydration Fever with Marked Increase in Serum Protein Concentration.*—The mother was a primipara, aged 28. The labor was prolonged and high forceps were applied under ether anesthesia. A large baby weighing 4,430 gm. was delivered. The mother's temperature was about 37.8 C. (100 F.) for the first three days after delivery, after which it rose to 39.5 C. (103 F.). On the fifth day, a small pelvic abscess was opened and drained, and the temperature gradually fell, reaching normal on the twelfth day. The mother left the hospital on the seventeenth day feeling well.

The baby weighed 4,430 gm. at birth. During the first three days after birth he lost 550 gm. His temperature, which up to the third day had been normal, rose to 39.7 C. (103.4 F.). The skin was very loose, but not inelastic.

The serum protein concentration was 9.10 per cent., rising later in the day to 9.40. The baby continued to lose weight between the third and fourth days, losing a total of 700 gm. The temperature was still elevated (39.2 C.) and the serum proteins were 9.30 per cent.

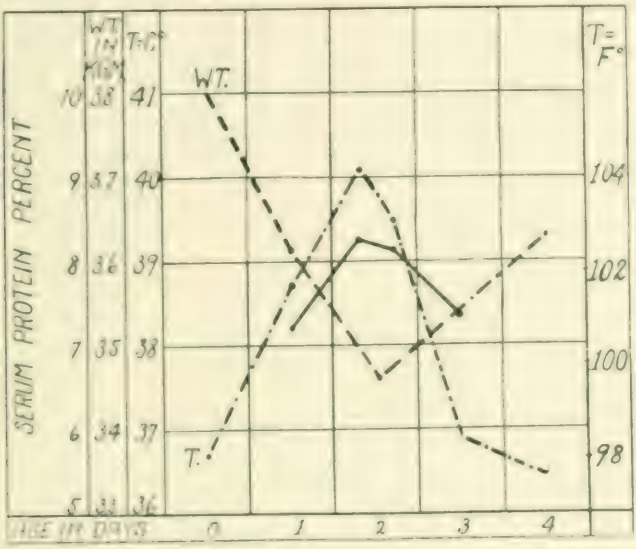

Fig. 4 (Case 3).—The relation between temperature, weight loss and serum protein per cent. (plasma concentration) in dehydration fever. The loss of weight is accompanied by a rise of temperature and an increase in the serum protein per cent. The temperature and serum proteins fall on the third day as the weight gain starts. In this baby the fever occurred within thirteen hours after birth.

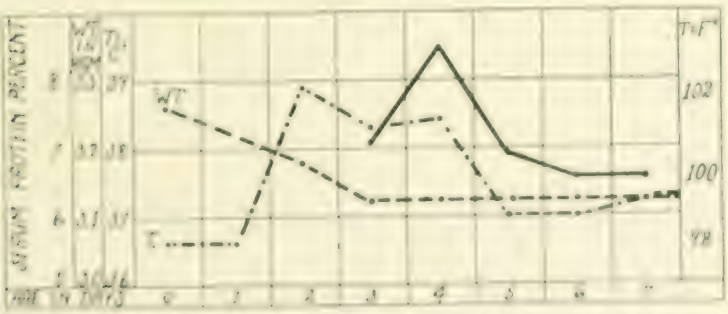

Fig. 5 (Case 5).—Dehydration fever in a new-born baby who has lost only 50 gm. The loss of a few grams is accompanied by a rise of temperature and an increased serum protein concentration. The temperature falls at the same time as the serum proteins.

On the fifth day the temperature dropped to 38 C. (100.4 F.). The serum proteins fell to 8.80 per cent. and the weight increased 10 gm. On the sixth day the temperature fell to normal, and remained there during the remainder of the baby's stay in the hospital. The serum proteins also fell from 8.80 on the fifth day to 7.80 on the sixth day, after which observations were discontinued.

Case 5 (Fig. 5).—*Dehydration Fever Unassociated With a Large Weight Loss.*—The mother was a primipara, aged 22. Delivery was instrumental (median forceps). The mother's temperature was normal until the fifth day postpartum, when it rose to 38.3 C. (101 F.), after which it remained elevated until the thirteenth day. It then dropped to normal and remained there until the mother's discharge from the hospital on the twentieth day postpartum.

The baby weighed 3,260 gm. at birth. Nothing abnormal was noted until the second day after delivery, when the baby's temperature rose to 38.9 C. (102.2 F.). He had lost only 80 gm. The patient was first seen on the following day (third day). He had lost an additional 60 gm. (total loss, 140 gm.); his temperature was 38.3 C. (101 F.), and the skin and plasma were dehydrated (serum protein per cent., 7.09). On the next day the fever persisted, the serum protein per cent. rising to 8.49. Between the fourth and fifth days, the temperature and serum protein per cent. fell to normal. There was no increase in weight. The subsequent course was normal.

Case 6 (Fig. 6).—*Severe Dehydration Fever. Fall in Temperature and Serum Concentration Following the Administration of Fluids.*—This was the mother's third pregnancy. Delivery and postpartum course were normal.

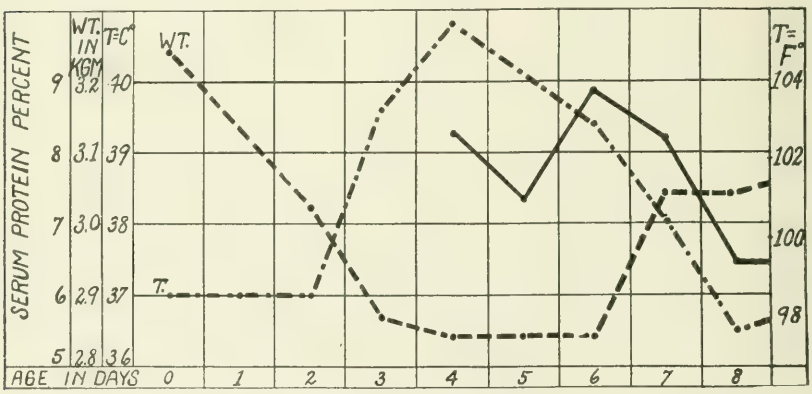

Fig. 6 (Case 6).—The relation between temperature, weight loss and serum protein per cent. (plasma concentration) in a severe case of dehydration fever. This case, like the others, shows the rise of temperature and increase in serum protein per cent. during the weight loss after birth. The serum proteins fall to normal as the temperature drops between the sixth and seventh days.

The baby weighed 3,240 gm. at birth. On the third day, after a loss of 370 gm., he developed fever which persisted until the eighth day, when it returned to normal. On the fourth day, the temperature was 40.8 C. (105.4 F.). During the febrile period the serum protein per cent. was high—8.89 on the sixth day. At this time, water was given by gavage (190 c.c.), and the nurses were instructed to give the baby water frequently during the night. On the following day (seventh day), the temperature fell to 38 C. (100.2 F.), and on the eighth day it was normal. With the fall in temperature the serum protein concentration dropped to normal, remaining there during the rest of the period of observation. The skin, which was inelastic during the fever, returned to normal, when the weight gain started between the sixth and seventh days.

Case 7 (Fig. 7).—*Fever in the Baby Associated with a Febrile Affection in the Mother. Intermittent Fever in the Baby for Twenty-Seven Days After Birth. No Increase in Serum Protein Concentration.*—The mother was a primipara, 21 years of age. Labor was normal. On the afternoon of the delivery her temperature, which had been normal in the morning, rose to 38.5 C. (101 F.), and remained elevated, with slight remissions, for thirty-four days,

fluctuating between 36.8 C. (98.2 F.) and 39.1 C. (102.4 F.). She was discharged cured on the fortieth day postpartum. The diagnosis was phlebitis of the left femoral vein.

The baby weighed 3,900 gm. at birth. The temperature taken shortly after birth was 37.8 C. (100 F.). It gradually rose and on the second day was

Fig. 7 (Case 7).—The relation between temperature in the mother and temperature in the baby. The upper line represents the temperature curve of the baby, the lower the temperature curve of the mother. Note the parallelism in the two curves. In this baby the serum concentration, determined on the second and third days, was normal.

TABLE 2 (Case 8).—Fever in the Baby Associated with a Fever Attack in the Mother

	Baby					Mother	
Age, Days	Weight, Gm.	Temperature, C.	Serum Proteins, per cent.	Skin Elasticity	Remarks	Temperature, C.	Remarks
0	3,150						Fever attack
1		36.8		Normal	Jaundice	39.1	
2	3,150	38.2	7.20	Normal	Jaundice	38.2	
3	3,100	39.1	6.48	Normal	Jaundice	38.9	
4	3,100	38.1	6.72	Normal	Jaundice	37.5	
5	3,100	38.1	6.96	Normal	Normal	36.9	
6	3,100	38.4	6.48	Normal	Jaundice	36.9	
7	3,100	38.8	6.48	Normal	Jaundice	36.9	
8	3,100	38.8	6.96	Normal	Jaundice	36.9	
9	3,100	37.4	6.96	Normal	Jaundice	36.9	

39.7 C. (103.2 F.). By this time the baby had lost 300 gm., but the skin was normally elastic and the plasma showed no evidence of intoxication (serum protein per cent., 6.97). On the third day the temperature dropped to 38 C. (100.2 F.), the skin and plasma remaining as observed (serum protein per cent., 6.96). The temperature of the baby and mother continued to fluctuate for thirty-four days, during most of which time the baby gained well. Note the parallelism between the mother's temperature curve and the baby's (Fig. 7).

Case 8 (Table 2).—*Fever in the Baby Associated with a Febrile Affection in the Mother. No Increase in the Serum Protein Per Cent. Accompanying the Fever. Fall in Temperature on Weaning.*—The mother was a primipara, aged 24. There was no fever until the third day postpartum, when the temperature rose to 40.5 C. (105 F.), remaining at this high level with slight remissions for five days, after which the temperature continued at a lower level. The diagnosis was pelvic abscess, for which the patient was operated on.

The baby weighed 3,730 gm. at birth. His temperature was normal for three days after birth, during which time he lost 390 gm. On the fourth day, one day after the onset of fever in the mother, the baby's temperature rose to 38.5 C. (101.8 F.). It remained elevated until the baby was removed from the breast on the sixth day, after which it was normal for the rest of the baby's stay in the hospital. The serum protein per cent. did not rise above 7 per cent. during the two febrile days. There was no drop in serum proteins when the temperature returned to normal on the sixth day. The skin was normally elastic during the febrile period.

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OXYGEN THERAPY IN PREMATURE BABIES WITH ANOXEMIA

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OXYGEN THERAPY IN PREMATURE BABIES WITH ANOXEMIA*

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NEW YORK

By anoxemia is meant a condition in which the oxygen pressure in the systemic capillaries is abnormally diminished.[1] It is seen most frequently when the hemoglobin of the blood is less saturated with oxygen than normally. The difference between the amount of oxygen which the hemoglobin is capable of carrying (oxygen capacity) and the amount which it actually carries (oxygen content) is known as the oxygen unsaturation of the blood.

In normal adults Lundsgaard[2] found that the unsaturation of the venous blood varies from 2.7 to 9.0 c.c. of oxygen for each hundred cubic centimeters of blood, averaging 5.8 c.c. Our results with blood obtained from the longitudinal sinus of well infants (Table 1) are practically the same as those of Lundsgaard on blood from the median basilic vein of adults. The oxygen unsaturation varied from 5.1 to 8.3 c.c., averaging 6.7 c.c. Blood from a scalp vein is much more nearly saturated with oxygen than is longitudinal sinus blood. Arterial blood is normally about 95 per cent. saturated.[3]

METHODS

Oxygen capacity was calculated from the hemoglobin.[4] The oxygen content was determined by the Van Slyke and Stadie method.[5] The earlier estimations were made with the Van Slyke method.[6]

In cyanotic persons an increase in the oxygen unsaturation of the venous and arterial blood was demonstrated by Stadie[7] in pneumonia and by Harrop[8] in patients with uncompensated heart disease. Lunds-

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2. Lundsgaard, C.: Studies of Oxygen in the Venous Blood, I. J. Biol. Chem. **33**:133, 1918.

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7. Harrop, G. A.: The Oxygen and Carbon Dioxid Content of the Arterial and Venous Blood in Normal Individuals and in Patients with Anemia and Heart Disease, J. Exper. M. **30**:241 (Sept.) 1919.

gaard,[8] working with venous blood alone, obtained similar results. All three observers agree that cyanosis is closely related to an increase in the oxygen unsaturation of the blood.

Cyanosis is, therefore, distinct evidence of anoxemia. It occurs frequently in premature babies and may be associated with a number of different conditions, such as cerebral hemorrhage, pneumonia and sepsis. The cases of cyanosis with which this paper is concerned, however, are those which occur so frequently during the first few days of life in prematurely born babies and for which no assignable cause can be found, except a few atelectatic patches in the lungs. In these babies cyanotic attacks start soon after birth and recur more or less frequently for several days. If the baby lives through this period the attacks usually cease. Death, however, is an all too frequent sequel.

TABLE 1.—The Oxygen Unsaturation of Blood from the Longitudinal Sinus of Well Infants

Case	Oxygen Capacity-Volume per Cent.	Oxygen Content-Volume per Cent.	Oxygen Unsaturation	
			Volume per Cent.	Percentage
1	15.1	7.9	7.2	48
2	15.1	9.2	5.9	39
3	16.4	11.3	5.1	45
4	14.4	8.5	5.9	41
5	16.5	9.1	7.4	45
6	14.9	6.7	8.2	55
7	15.1	7.2	7.9	52
8	13.7	6.6	7.1	52
9	13.9	7.5	6.4	46
10	18.0	11.3	6.7	37
11	20.2	13.0	7.2	36
12	14.1	8.9	5.2	37
13	16.7	10.9	5.8	35

The cyanosis in premature babies is usually extreme and is accompanied, as in adults, by an increase in the oxygen unsaturation of the blood (Compare case histories). During the cyanotic attack the respirations become progressively slower and finally cease. The heart also beats slower and becomes weaker; but it usually continues to beat for several minutes after respiration has ceased.

THE MODE OF PRODUCTION OF ANOXEMIA IN PREMATURE BABIES

According to Holt[9] expansion of the lungs of the new-born is a gradual process requiring several days for its completion. In small, frail babies full expansion of the lungs may be delayed for several weeks. As a consequence, the blood flowing through the walls of the collapsed alveoli is poorly or not at all oxygenated, whereas in the expanded

8. Lundsgaard, C.: Studies of Oxygen in Venous Blood, IV, J. Exper. M. **27**:219 (Sept.) 1918.

9. Holt, L. E.: Diseases of Children, 1919, p. 69.

portion of the lungs the blood is normally arterialized. The mixed arterial blood coming from the lungs, therefore, is incompletely oxygenated, and anoxemia results.

Evidence of the anoxemia in premature babies is found in the type of breathing so frequently seen in these babies. It is a matter of common clinical observation that the breathing in prematurely born infants is irregular both in rate and depth. Recently Eckstein and Rominger [10] obtained graphic records of the respiration. They found that it may be distinctly periodic in type and describe three varieties of periodicity. One type is that known as Cheyne-Stokes breathing, in which periods of hyperpnea are followed by periods of apnea. They have seen apneic periods lasting as long as ten seconds. In other cases, deep breaths alternate with shallow ones, the entire curve showing a wavelike rise and fall. The latter phenomenon they interpret as due to changes in the tone of the diaphragm. In a third type rapid, shallow respirations alternate with slow, deep ones.

According to Douglas and Haldane [11] periodic breathing is due to anoxemia. The stimulus of oxygen want, expressed physiologically by the decrease in the oxygen saturation of the blood, together with the carbon dioxid present, results in excitation of the respiratory center and hyperpnea. The hyperpnea relieves the oxygen want, and the breathing quiets down only to start up again when the oxygen deficiency reaches the stimulating point once more. Pembrey and Allen [12] have shown that Cheyne-Stokes breathing may be abolished by giving oxygen, thereby proving, Haldane believes, that this type of breathing is due to oxygen want.

EXPERIMENTAL STUDIES

The effect of oxygen on anoxemia in prematurely born babies was studied by comparing the saturation of the blood and the clinical condition before and after the administration of oxygen. The two babies selected for this study showed marked evidence of anoxemia. A large group of cases has been observed clinically during the past three years, but it did not seem advisable to make blood determinations.

Method of Administering Oxygen to Babies.—In order that oxygen therapy may be of value, the oxygen must be properly given. The funnel method, which has been so widely used, is practically useless. Meltzer [13] estimated that by this method the inspired air is enriched

10. Eckstein, A., and Rominger, E.: Beiträge zur Physiologie und Pathologie der Atmung, Zeitschr. f. Kinderh. **28**:1, 1921.

11. Douglas, C. G., and Haldane, J. S.: The Causes of Periodic or Cheyne-Stokes Breathing, J. Physiol. **38**:401 (June) 1909.

12. Pembrey, M. S., and Allen, D. W.: Observations Upon Cheyne-Stokes Respiration, J. Physiol. **32**:XVIII, 1905. (Proc. Physiol. Soc.)

13. Meltzer, S. J.: The Therapeutic Value of Oral Rectinoid Insufflation of Oxygen, J. A. M. A. **69**:1130 (Oct. 6) 1917.

by not more than 2 per cent. of oxygen. Haldane [14] devised an apparatus by which oxygen could be accurately and economically added to the inspired air. Oxygen was also given during the recent war with some success through a nasal catheter.[15] Excellent results have been obtained by various workers [16] with the oxygen chamber. Barach and Woodwell [17] found a rubber mouthpiece an effective means of giving oxygen.

In prematurely born infants oxygen may be given effectively by means of two fine rubber catheters inserted into the nostrils. The catheters are well lubricated and connected to the oxygen tank by means of a Y tube. The oxygen may also be given through a rubber tube about 1 cm. in diameter, inserted into the mouth. The rubber tube is held in position by a glass collar which fits snugly over the tube. The collar is held in place with tape, which is tied back of the baby's head. Since the small babies move very little, the collar and tube are easily kept in place. Such a collar eliminates the need of a nurse in constant attendance during the oxygen administration. Occasionally when oxygen is given in this way, it is swallowed, and the abdomen becomes distended. In such cases, of course, the oral route should be abandoned.[18]

REPORT OF CASES

Case 1.—*History.*—A baby boy, who was delivered normally and weighed 1,690 gm., began to have attacks of cyanosis shortly after birth, the attacks usually occurring soon after a feeding. The blood oxygen determinations were made one day after birth. At this time the baby was deeply cyanotic, the heart rate 20 per minute and the rhythm regular. The breathing was very shallow and irregular. The physical examination otherwise was negative.

Treatment.—Oxygen was given through a tube inserted into the mouth. After a few minutes the baby became bright pink, the respirations became deeper and the heart sounds stronger. The baby continued to have attacks of cyanosis for the next few days, particularly after his feedings. He was treated each time with oxygen, to which he reacted promptly. He was discharged from the hospital cured, and when last seen was 6 months old and apparently well, except for slight malnutrition.

Comment.—In this case the oxygen unsaturation which was very high before the oxygen administration (14.8 c.c. for each hundred cubic

14. Haldane, J. S.: The Therapeutic Administration of Oxygen, Brit. M. J. **1**:181 (Feb. 10) 1917.

15. Stokes, quoted by Cummins: Proc. Roy. Med. Soc. **13**:59, 1920.

16. Barcroft, J.; Hunt, G. H., and Dufton, D.: The Treatment of Chronic Cases of Gas Poisoning by Continuous Oxygen Administration in Chambers, Quart. J. M. **13**:179, 1920. Shufflebotham, F., and Sowry, G. H.: Proc. Roy. Med. Soc. **13**:59, 1920. Stadie, W. C.: The Treatment of Anoxemia in Pneumonia in an Oxygen Chamber, J. Exper. M. **35**:337 (March) 1922.

17. Barach, A. L., and Woodwell, M. N.: Studies in Oxygen Therapy with Determination of Blood Gases, Arch. Int. Med. **28**:367 (Oct.) 1921.

18. These methods may also be used in older infants. Often, however, the babies struggle against the tubes. In these cases the oxygen may be given in a tent constructed from sheets.

centimeters) fell to normal (5.5 c.c.) after the oxygen was given. The results of the blood examinations are shown in Table 2.

Case 2.—*History.*—A boy, the first child, was delivered normally and weighed 2,030 gm. Except for his small size he seemed normal. On the second day after birth it was noticed that he had attacks of cyanosis; at times he almost ceased to breathe. He was restored each time with counter irritation (mustard baths) and artificial respiration. The attacks became more and more frequent, and it was becoming increasingly difficult to revive him.

Examination.—The baby was seen during an attack on the third day. He was extremely cyanotic, spontaneous respiration having ceased. The heart rate was 15 per minute, and the sounds only faintly audible. There was sclero-edema of the skin over the abdomen and thighs.

Treatment.—Artificial respiration was used, but the apnea and cyanosis persisted. Oxygen was then given through a rubber tube in the mouth, and

TABLE 2.—Increase in Blood Oxygen of Case 1 After the Administration of Oxygen

	Oxygen Capacity, Volume per Cent.	Oxygen Content, Volume per Cent.	Oxygen Unsaturation, Volume per Cent.	Color
Before oxygen	27.9	13.1	14.8	Extreme cyanosis
After oxygen	27.9	22.4	5.5	Rosy pink

TABLE 3.—Increase in Blood Oxygen of Case 2 After the Administration of Oxygen

	Oxygen Capacity, Volume per Cent.	Oxygen Content, Volume per Cent.	Oxygen Unsaturation, Volume per Cent.	Color
Before oxygen	28.8	7.5	21.3	Deep cyanosis
After oxygen	35.3	7.6	7.7	Rosy pink

the artificial respiration continued. Within a few minutes the baby began to breathe spontaneously, the respirations becoming markedly periodic in type. As the oxygen was continued the baby became rosy pink in color, the respirations became more regular and the heart sounds improved in quality, the rate rising to 60. The oxygen unsaturation of blood from the longitudinal sinus fell from 13.1 to 7.7 c.c., which is within normal limits (Table 3). The results of the blood determinations are shown in Table 3.

The baby had several other attacks of cyanosis during the day and was revived each time with oxygen. The sclero-edema extended to the face and arms, and the baby died during the night. Necropsy was not permitted. There was no evidence of organic disease at any time aside from the sclero-edema.

COMMENT

In the two cyanotic infants studied the oxygen unsaturation of the venous blood before treatment was markedly increased, indicating a severe degree of anoxemia. The administration of oxygen resulted, in both instances, in a prompt return of the oxygen saturation to normal. The cyanosis disappeared, abnormal respiration was abolished and the heart rate rose to normal. One of the two infants treated was 6 months

old when last seen and was apparently well, except for slight malnutrition. The other baby, who had sclero-edema at the time of treatment, died some time after the oxygen inhalations were discontinued.

During the past three years a large number of cyanotic premature infants have been treated with oxygen inhalations. The response to the oxygen is usually prompt, and but a few minutes are necessary before the cyanosis disappears and the character of the respirations changes. It is difficult to gage with any degree of accuracy the permanent value of oxygen to the babies. It did seem that, in general, when oxygen was administered early, the subsequent cyanotic attacks were fewer in number and more readily amenable to treatment.

With the methods employed (nasal catheters, mouth-tube), the oxygen could necessarily be given only over comparatively short periods of time. Though it was usually effective in remedying the immediate attacks of cyanosis, as a rule, the attacks recurred. In order that the full benefit of oxygen therapy may be obtained, it should be given over a long period of time. For this purpose the oxygen chamber is almost ideal.

SUMMARY AND CONCLUSIONS

1. The oxygen unsaturation of blood from the longitudinal sinus of well infants varies from 5.1 to 8.3 c.c., averaging 6.7 c.c.

2. The oxygen unsaturation of longitudinal sinus blood in two prematurely born babies with marked cyanosis was 14.8 and 13.1 c.c., respectively.

3. These two prematurely born babies with marked anoxemia, as indicated by the cyanosis and the increase in the oxygen unsaturation of the venous blood, were treated with oxygen inhalations. In both instances the cyanosis disappeared and the saturation of the venous blood rose to normal.

4. Oxygen may be given effectively to prematurely born babies through nasal catheters or through a rubber tube inserted into the mouth

I wish to express my thanks to Dr. Jesse F. Sammis and to Dr. Louis C. Schroeder for many helpful suggestions in the course of the work.

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THE ESTIMATION OF THE VOLUME OF BLOOD IN NORMAL INFANTS AND IN INFANTS WITH SEVERE MALNUTRITION*

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No study on fluid regulation in the body can be complete without some knowledge of the total amount of circulating fluid. Because of the large quantities of blood hitherto necessary to estimate the blood volume, few determinations have been made in infants. It was primarily with the purpose of obtaining more data on the subject that this investigation was undertaken.

The method used for estimating the volume of blood was a micro-modification of the method of Keith, Rowntree, and Geraghty [1] as improved by Hooper, Smith, Belt and Whipple.[2] A known amount of a nontoxic, slowly diffusible dye is injected into a vein, is allowed to circulate for a few minutes and a specimen of blood withdrawn. By determining the concentration of the dye in the plasma, the plasma volume may be calculated. The total blood volume may be computed from the hematocrit reading.

In normal adults the total volume of blood is about 9 per cent. of the body weight, and the plasma volume about 5 per cent.[3] In normal infants Lucas and Dearing [3] found that the values were higher and varied much more widely than in adults. According to these observers, in the new-born the volume of blood varies from 10.7 to 19.5 per cent. of the body weight, averaging 14.7. The plasma volume varies from 4.2 to 7.7 per cent. of the body weight, averaging 5.9. In older infants the blood volume ranges from 9.0 to 12.6 per cent. of the body weight averaging 11.0. The plasma volume varies from 5.7 to 7.8 per cent. of the body weight, averaging 6.7.

Marriott and Perkins [4] determined the volume of blood in normal infants and in infants with marasmus. They found that in seven

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1. Keith, N. M.; Rowntree, L. G., and Geraghty, J. T.: A Method for the Determination of Plasma and Blood Volume, Arch. Int. Med. **16**:547 (Oct.) 1915.

2. Hooper, C. W.; Smith, H. P.; Belt, A. E., and Whipple, G. H.: Experiments Centred on a Dye Blood Volume Method, Am. J. Physiol. **51**:493 (March) 1920.

3. Lucas, W. P., and Dearing, H. F.: Blood Volume in Infants: Estimated by the Vital Dye Method, Am. J. Dis. Child. **21**:196 (Jan.) 1921.

4. Marriott, W. M., and Perkins, J. F. (quoted by Marriott): Some Phases of the Pathology of Nutrition in Infancy, Harvey Lectures, 1920-1921, p. 121.

normal infants the volume of blood varied from 8.0 to 10.8 per cent. of the body weight. In eleven infants with marasmus the values ranged from 4.0 to 10.4 per cent. of the body weight. They state that the higher values were obtained in infants who might be considered as convalescing from the marasmus. They conclude that the volume of blood in infants with marasmus is lower that in normal infants.

PROCEDURE AND METHODS

The blood volume was determined in a group of normal infants and infants with severe malnutrition. Estimations of the serum protein concentration and hemoglobin percentage were made at the same time.

Determinations were made from three to four hours after a feeding. To avoid diurnal variations the blood specimens were always taken at the same time of the day (between 1 and 2 p. m.). Specimens for hemoglobin and serum protein estimations were obtained immediately before the dye was injected. Hemoglobin was determined by the carbon monoxid method of Palmer.[5] The serum protein concentration was determined with the Abbe refractometer. The technic used was similar to that described in previous papers.[6] The calculations were made according to Reiss.[7]

The following micromodification of the dye method of Keith, Rowntree and Geraghty [1] was used to determine the volume of blood: A 1.5 per cent. solution of brilliant vital red in saline was prepared. This solution was sterilized before each set of determinations. Two cubic centimeters of blood were drawn into a dry syringe and delivered into a heavy walled hematocrit tube, 12.5 cm. in length and 0.6 cm. in diameter. The graduated tubes were calibrated in divisions of 0.04 c.c. and contained 0.4 c.c. of 1.6 per cent. sodium oxalate solution to prevent clotting. The oxalate and blood were mixed by inverting. The plasma obtained in this way was later used in the preparation of the standard.

Without removing the needle from the vein, 1 c.c. of dye, prepared in the manner described above, was injected.[8] Four minutes later a fresh needle was introduced and 2 c.c. of blood again withdrawn. The blood obtained in this way was delivered into a tube similar to the first and also containing 0.4 c.c. of sodium oxalate solution.

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5. Palmer, W. W.: The Colorimeter Determination of Hemoglobin, J. Biol. Chem. **33**:119 (Jan.) 1918.

6. Bakwin, H.: Dehydration in New-Borns, Am. J. Dis. Child. **24**:497 (Dec.) 1922.

7. Reiss, E.: Die refraktometrischen Untersuchungen und ihre Ergebnisse für die Physiologie und Pathologie des Menschen, Ergebn. d. inn. Med. u. Kinderh. **10**:531, 1913.

8. The amount of dye used for injection may be varied according to the weight of the subject. The variation in the weight of the babies studied was comparatively small, and we therefore used 1 c.c. except in infants under 3 kg. in whom 0.5 c.c. was used.

Both tubes were then centrifuged for twenty minutes at 1,500 revolutions per minute and hematocrit readings made in the tubes. The supernatant fluid (plasma and oxalate solution) was pipetted off into clean test tubes. One cubic centimeter of the dye-stained plasma oxalate mixture was added to 2 c.c. of normal saline and matched in a colorimeter (using microcups and microplungers) against the standard mixture. The standard mixture consisted of 1 c.c. of saline, 1 c.c. of plasma oxalate solution obtained before the dye was injected and 1 c.c. of dilute dye solution.[9] The dilute dye solution was prepared by making up 1 c.c. of 1.5 per cent. dye solution to 400 c.c. with saline. This was prepared before each set of determinations.

The calculations were as follows:

$$\text{Plasma volume} = \frac{R}{15} \times 400 \times \frac{P - 0.4}{P} \times D$$

$$\text{Blood volume} = \frac{\text{plasma volume}}{\text{plasma per cent.}} \times 100$$

Corpuscular volume = blood volume minus plasma volume

where

R = colorimeter reading with the standard at 15.

P = amount of dye-stained plasma oxalate solution in the hematocrit tube

D = c.c. of dye injected

$$\text{Plasma per cent.} = \frac{P - 0.4}{\text{Total amount of fluid in tube minus } 0.4} \times 100$$

This is probably as accurate as the original method, since the errors due to measuring the smaller amounts of fluid are well within the limits of error inherent in the method.[10]

The longitudinal sinus was used in all the determinations. A short beveled, 20 gage needle, 6 mm. in length, proved entirely satisfactory.

All the babies used in this study were artificially fed. It was not possible to obtain a large series of strictly normal babies. The "normal"

9. In the experiments of Eaton and Dearing,[3] sodium oxalate solution was added to the tube containing the blood obtained before the dye was injected but not to the second tube. The actual amount of plasma in their standard tubes was therefore from 25 to 40 per cent. less than in the "unknown" tube. We have found that even small discrepancies in the actual amount of plasma added cause difficulty in the colorimeter reading. The plasma of the new-born is often high colored. In older infants, partial sera are not infrequently encountered.

10. The exact manner in which the dye is removed from the body is unknown. Keith, Rountree and Geraghty, using coal red, found small amounts in the urine. With the technique used in these experiments (brilliant cresyl blue) the urine was always negative. In the dogs, however, dye was regularly present in the urine as early as ten hours after the injection and as late as fifteen days afterward.

babies were healthy in the sense that they were not suffering from any acute illness. Some of them were slightly underweight. None of the babies had fever.

RESULTS

Repeated determinations of the blood, plasma and corpuscular volumes on the same patient were made in sixteen instances (Table 1). Two of the infants were markedly underweight (Cases 537, 542). Two others were anemic (Cases 548, 549). The rest of the babies were fairly normal.

TABLE 1.—*The Results of Repeated Determinations of the Blood Volume, Etc., in Infants*

			Total Volume			Volume per Kg. Body Weight				
Case	Age, Months	Weight, Kg.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Hemoglobin, Gm. per 100 C.c.	Serum Protein, per Cent.
504	¾	3.47	344	204	140	99	59	40	12.9	—
	1½	3.46	334	214	120	97	62	35	11.2	—
505	1	2.76	353	198	155	128	71	57	14.3	—
	1½	2.93	281	178	103	96	61	35	11.7	—
	3½	3.93	372	243	129	94	61	33	—	—
506	1½	2.78	413	185	228	148	66	82	16.8	—
	1¾	3.04	360	190	170	117	63	54	13.8	4.90
513	2	3.72	401	272	129	108	69	39	11.7	5.49
	3	4.20	377	242	135	90	58	32	10.4	—
532	2	2.79	326	210	116	117	75	42	9.5	5.31
	2½	2.82	364	236	128	129	84	45	11.2	—
510	2	3.47	325	228	97	94	66	28	9.9	5.31
	4	3.58	403	258	145	113	72	41	12.9	—
537	3	2.93	334	216	118	115	74	41	10.3	5.95
	3½	2.93	347	218	129	118	74	44	11.2	—
536	3	2.87	353	242	111	126	85	41	—	7.11
	3½	2.98	366	248	118	123	83	40	9.0	6.53
	3¾	3.38	396	250	146	117	74	43	12.6	6.53
519	3½	3.90	434	270	164	112	69	43	12.5	7.11
	3¾	4.32	452	282	170	105	65	40	—	—
517	3½	4.35	437	284	153	101	65	36	10.1	—
	4	4.52	403	272	131	89	60	29	9.7	5.84
523	5	5.48	457	290	167	83	53	30	10.5	—
	5½	5.77	524	344	180	91	60	31	10.6	6.17
	6	6.03	517	326	191	86	54	32	—	—
	6½	6.17	575	359	216	93	58	35	10.7	6.59
542	5	2.90	228	161	67	79	56	23	9.2	5.78
	5½	2.90	276	185	91	95	64	31	9.6	5.89
	6	3.04	294	206	88	97	68	29	10.1	6.24
	7	3.41	342	238	104	100	70	30	9.8	—
524	5½	5.12	479	303	176	94	59	35	11.8	—
	5¾	4.97	520	327	193	105	66	39	12.7	—
546	6½	4.67	444	302	142	95	65	30	8.6	7.79
	7½	4.66	483	314	171	104	67	37	10.7	7.93
	7¾	4.88	503	326	177	103	67	36	9.7	7.56
548	7	3.41	300	225	75	88	66	22	7.2	—
	7½	3.54	422	308	114	115	85	30	8.1	—
549	9	4.80	446	334	112	93	70	23	5.2	6.87
	9½	4.83	467	356	111	97	74	23	6.1	7.17

In the three infants under 8 weeks of age on whom repeated determinations were made (Cases 504, 505, 506) a drop in the absolute volume of corpuscles occurred. In Case 505, despite the fact that the baby gained 170 gm. in two weeks, the volume of red cells fell from 155 c.c. to 103 c.c. In Case 506, similarly, though the baby gained 250 gm. in weight during the week intervening between the two determinations, the volume of red cells fell from 228 c.c. to 170 c.c. In the only

infant under 8 weeks of age on whom Lucas and Dearing made repeated determinations (their Table 4, Case H. O.) a similar drop in the absolute volume of red cells from 175 c.c. to 134 c.c. occurred.

The volume of plasma in our cases showed little change during this period of life. It increased slightly in two cases and fell slightly in the third. In the patient studied by Lucas and Dearing there was a considerable increase in the plasma volume between the fifteenth and fiftieth days.

In all four infants the fall in red cell volume was accompanied by a drop in the hemoglobin percentage. It is known that the red cell count during this period falls rapidly. These results indicate that the fall in the hemoglobin percentage and red cell count during the first weeks of life is owing to an actual reduction in the number of circulating corpuscles and not to an increase in the plasma volume.

After the first weeks of life the volume of plasma and corpuscles increases steadily. It is interesting to note that this usually proceeds even though no significant gain in weight occurs (Table 1, Cases 532, 537, 542, 524, 546, 549).

The Relation Between the Volume of Blood and the Body Weight in Normal Infants.—A résumé of the results of estimations of the volume of blood, plasma and red cells together with other data is given in Table 2. In Charts 1, 2 and 3 the blood, plasma and corpuscular volumes per kilogram of body weight, respectively, are graphically represented in relation to age. The dots represent individual determinations. The continuous lines in Charts 1, 3, 4 and 6 represent the average at different ages as obtained by the method of least squares.

The volume of blood per kilogram of body weight in normal infants varies from 71 c.c. to 148 c.c., averaging 101 c.c. The values obtained, like those of Lucas and Dearing, are not only higher than in adults but they vary more widely. It is of interest that the highest figures were obtained during the new-born period (Chart 1). There is a gradual fall as the age increases but at 7 months the blood volume is still relatively higher than in adults. The variations in results are also more marked during the new-born period than later in infancy.

That the decrease in the amount of blood per kilogram of body weight as the age increases is due to a diminution in the volume of red cells is apparent from Charts 2 and 3. The volume of red cells is relatively high during the first weeks of life. It falls abruptly at first more gradually later, the curve for the corpuscular volume running in a general way parallel to that of the total blood volume.

The volume of plasma per kilogram of body weight (Chart 2) shows wide variations (38 c.c. to 72 c.c., averaging 61 c.c. per kilogram of body weight), particularly during the new-born period. This is

in marked contrast to the relative constancy of the plasma volume in adults.[11] Recent studies tend to show that, in adults of the same nutritional condition, despite wide variations in the volume of corpuscles, the plasma volume remains fairly constant. Bock [11] points out that even in such widely different conditions as polycythemia and pernicious anemia, though the red cell volume varies greatly, the plasma volume remains relatively unchanged.

TABLE 2.—*The Blood Volume in Normal Infants*

			Total Volume			Volume per Kg. Body Weight				
Case	Age	Weight, Kg.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Hemoglobin, Gm. per 100 C.c.	Serum Protein, per Cent.
500	12 days	2.40	253	91	162	105	38	67	19.4	—
501	2 wks.	3.04	358	222	136	118	73	45	12.8	5.49
502	2 wks.	2.84	304	152	152	107	54	53	—	6.01
503	3 wks.	3.60	402	186	216	113	52	61	18.4	5.78
504	3 wks.	3.47	344	204	140	99	59	40	12.9	—
505	1 mo.	2.76	353	198	155	128	71	57	14.3	—
518	5 wks.	2.78	294	161	133	106	57	48	13.8	5.14
504	5 wks.	3.39	386	211	175	114	62	52	13.3	5.78
504	5 wks.	3.46	334	214	120	97	62	35	13.1	—
506	6 wks.	2.79	413	185	228	148	66	82	16.8	—
505	6 wks.	2.93	281	178	103	96	61	35	11.7	—
509	6 wks.	3.64	372	244	128	102	67	35	10.3	6.30
506	7 wks.	3.04	360	190	170	117	62	54	13.8	4.90
510	2 mos.	3.47	325	228	97	94	66	28	9.9	5.34
511	2 mos.	4.85	448	282	166	93	58	34	11.3	5.66
512	2 mos.	4.09	299	206	93	73	50	23	—	—
513	2 mos.	3.72	401	272	129	108	69	39	11.7	5.49
513	3 mos.	4.20	377	242	135	90	58	32	10.4	—
514	3 mos.	3.42	368	236	132	108	69	39	12.7	5.37
515	3 mos.	4.83	453	310	143	94	64	30	10.4	5.95
517	3 mos.	4.35	437	284	153	101	65	35	10.1	6.70
505	3 mos.	3.98	372	243	129	94	61	33	—	—
519	3 mos.	3.90	434	270	164	112	69	43	12.5	7.11
519	4 mos.	4.32	452	282	170	105	65	40	—	—
510	4 mos.	3.58	403	258	145	113	72	41	11.4	—
517	4 mos.	4.52	403	272	131	89	60	29	9.7	5.84
521	5 mos.	5.38	515	320	195	96	60	36	10.6	7.11
575	5 mos.	4.99	478	303	175	96	61	35	12.8	5.37
523	5 mos.	5.48	457	290	167	83	53	31	10.5	—
523	5½ mos.	5.77	524	344	180	91	60	31	10.6	6.07
524	5½ mos.	5.12	479	303	176	94	59	35	11.8	....
524	5¾ mos.	4.97	520	327	193	105	66	39	12.7	....
523	6 mos.	6.03	517	326	191	86	54	32	....	....
523	6½ mos.	6.17	575	359	216	93	58	35	10.7	6.59
525	7 mos.	5.62	408	270	138	71	48	23	—	6.65
528	10 mos.	6.53	534	320	114	82	49	33	9.4	—

It is probable that these wide variations in the relation between plasma volume and body weight in infants are due, in part at least, to the fact that the daily up and down fluctuations in the weight curve of an artificially fed infant do not represent the true weight of the baby but are due to changes in the water content of the tissues. Freund [12] studied the nitrogen and chlorin balance in a series of artificially fed infants and found that during days of rapid weight gain the nitrogen retention was sufficient to account for only a small part of the gain.

11. Bock, A. V.: The Constancy of the Volume of the Blood Plasma, Arch. Int. Med. **27**:83 (Jan.) 1921.

12. Freund, W.: Wasser und Salze in ihren Beziehungen zu den Körpergewichtsschwankungen der Säuglinge, Jahrb. f. Kinderh. **59**:421, 1904.

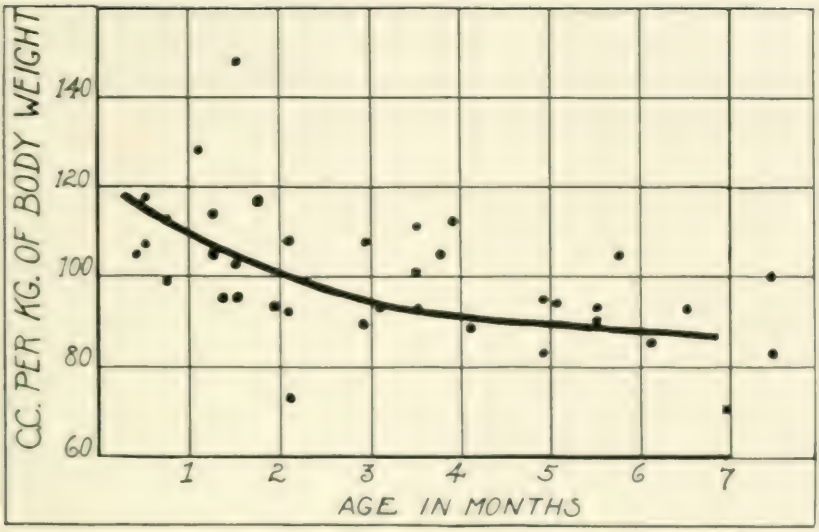

Chart 1.—The volume of blood per kilogram of body weight in relation to age in normal infants.

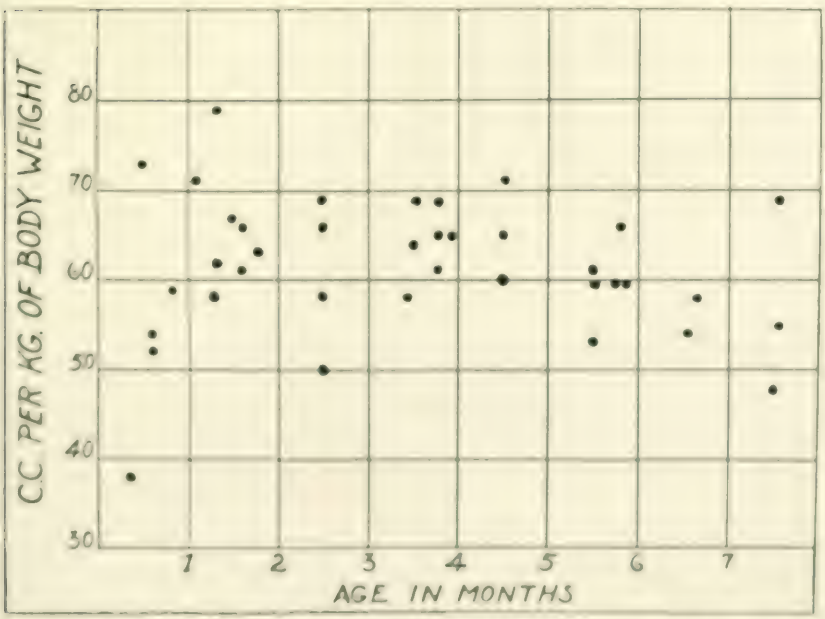

Chart 2.—The volume of plasma per kilogram of body weight in relation to age in normal infants.

That the major part of the weight increase was due to water retention was shown by a marked diminution in the elimination of chlorid and alkali salts. Moreover it has been found [13] that rapid weight increases in artificially fed infants are not accompanied by an increase in the water content of the plasma, thus indicating that the increased amount of fluid is held in the tissues and does not enter the blood.

TABLE 3.—*The Blood Volume in Infants with Severe Malnutrition*

			Total Volume			Volume per Kg. Body Weight				
Case	Age, Months	Weight, Kg.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Hemoglobin, Gm. per 100 C.c.	Serum Protein, per Cent.
529	2	2.61	282	171	111	108	66	42	6.44	6.53
530	2	2.99	276	182	94	92	61	31	10.0	6.24
531	2	2.80	235	153	82	84	54	30	—	—
532	2	2.79	326	210	116	117	75	42	9.53	5.31
532	2½	2.82	364	236	128	129	84	45	11.2	—
533	2½	3.04	330	244	86	109	81	28	8.5	5.25
534	3	3.18	325	214	111	105	67	38	10.7	5.43
536	3	2.87	353	242	111	126	85	41	—	7.11
537	3	2.93	334	216	118	115	74	41	10.3	5.95
537	3½	2.93	347	218	129	118	74	44	11.2	—
538	3½	3.97	314	204	110	79	51	28	9.6	5.95
536	3½	2.98	366	248	118	123	83	40	9.0	6.53
536	3¾	3.38	396	250	146	117	74	43	12.6	6.53
576	4	3.10	308	209	99	99	67	32	10.4	—
577	4	4.00	387	255	132	97	64	33	11.38	5.89
539	4	4.00	468	312	156	117	78	39	11.1	6.24
540	4½	4.80	405	272	133	84	57	27	10.0	7.11
541	5	4.00	490	313	177	123	79	44	10.7	6.36
542	5	2.90	228	161	67	79	56	23	9.2	5.78
542	5½	2.90	276	185	91	95	64	31	9.6	5.89
542	6	3.04	294	206	88	97	68	28	10.1	6.24
543	6	3.64	354	225	128	97	62	35	10.2	7.52
544	6	3.58	366	250	116	102	70	32	12.8	5.37
545	6	4.54	401	269	132	88	59	29	9.4	6.36
546	6½	4.67	444	302	142	95	65	30	8.6	7.79
547	7	4.60	390	252	138	84	55	29	7.87	4.85
526	7	4.09	341	224	117	84	55	28	10.4	—
542	7	3.41	342	238	104	100	70	30	9.8	—
548	7	3.41	300	225	75	88	66	22	7.17	—
548	7½	3.64	422	308	114	115	85	30	8.05	—
549	7½	4.35	437	298	139	101	69	31	9.1	6.81
546	7½	4.65	483	314	169	104	67	37	10.7	7.93
546	7¾	4.88	503	326	177	103	67	36	9.7	7.56
567	9	4.30	493	306	187	115	71	44	11.1	7.05
559	9	4.80	445	334	111	93	70	23	5.2	6.87
559	9½	4.83	467	356	111	97	74	23	6.1	7.17
550	12	5.10	553	338	215	108	66	42	9.7	7.11
551	14	3.50	309	221	88	88	63	25	7.9	4.07
552	14½	3.05	325	224	101	107	74	33	—	6.12
553	15	6.24	630	420	110	101	67	34	—	7.81

The Volume of Blood in Infants with Severe Malnutrition.—A résumé of the results in infants with severe malnutrition is given in Table 3. In Charts 4, 5 and 6 the blood, plasma and corpuscular volumes, respectively, per kilogram of body weight are represented according to age. The crosses indicate individual determinations in marantic babies. The dots in Chart 5 represent individual determinations in normal babies and are inserted for comparison. The heavy continuous lines in Charts 4 and 6 are transcribed from Charts 1 and 3

13. Bakwin, H.: The Water Content of Infants' Blood During Periods of Rapid Increase in Weight, Am. J. Dis. Child. **25**:406 (May) 1923.

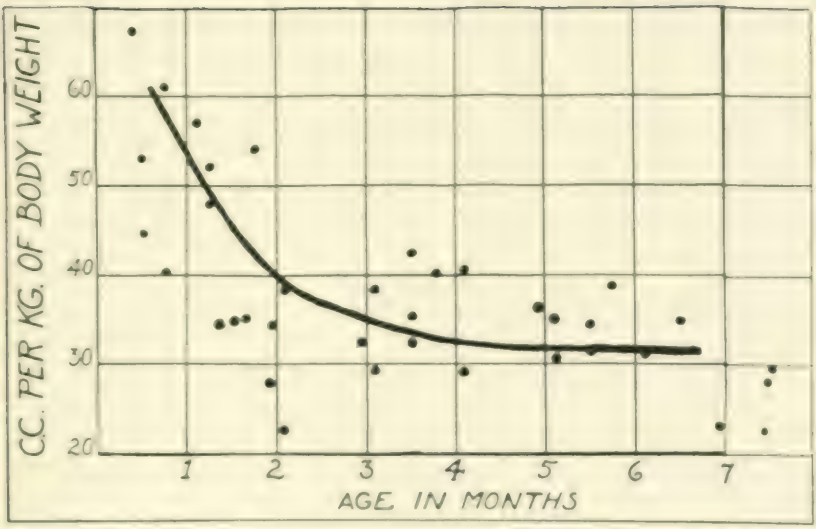

Chart 3—The volume of red cells per kilogram of body weight in relation to age in normal infants.

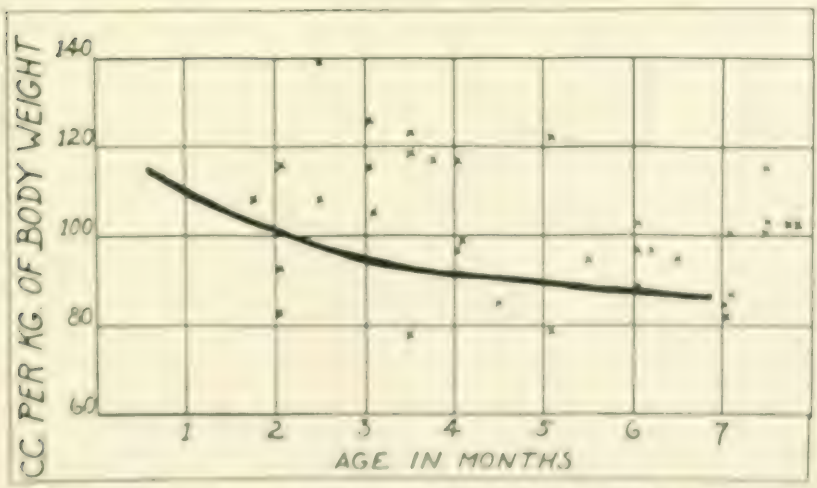

Chart 4—The volume of blood per kilogram of body weight in relation to age in infants with severe malnutrition.

and represent the averages for the blood and red cell volumes per kilogram of body weight at different ages as obtained by the method of least squares.

The average value obtained for the infants with severe malnutrition varies little from the normal average (103 c.c. of blood per kilogram of body weight for infants with marasmus, 101 c.c. for normal infants). However, since, in computing the normal average, the values obtained in infants during the first weeks of life when the blood volume is high were included, the averages for normal and marantic infants are not directly comparable. Most of the normal babies were under 4 months, whereas most of the marantic infants were past this age. For the same age period the blood volume in infants with marasmus is relatively higher than in normal infants (Chart 4). This is true in spite of the fact that most of the infants with marasmus were more or less anemic (hemoglobin under 10 gm. per hundred cubic centimeters of blood), a factor which would tend to lower their blood volume.

The plasma volume in marantic infants is relatively higher than in normal infants. The average value for the plasma volume in infants with marasmus is 69 c.c. per kilogram of body weight, for normal infants 61 c.c.

The Relation Between the Volume of Blood and the Body Surface in Infants.—According to Dreyer and Ray [14] the volume of blood in mammals is proportional to the body surface and not to the body weight. They believe that the practice of expressing the blood volume in percentage of body weight is misleading, particularly when individuals of different nutritional conditions are compared. Since adipose tissue is comparatively nonvascular, thin individuals of the same length and muscular development should have a larger blood volume in relation to the body weight than fat individuals. The bodies of the infants with malnutrition obviously contained less fat than normal babies, and one would therefore expect them to have a higher blood volume in relation to body weight than normal infants.

The blood volume was computed in relation to body surface [15] in nineteen cases. Whereas in adults the amount of blood per square meter of body surface averages 3.12 liters,[16] the average value for infants is 1.7 liters. Though the blood volume in an infant, therefore, is large in proportion to the body weight it is much smaller than the adult in relation to body surface.

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14. Dreyer, G., and Ray, W.: Phil. Tr. Roy. Soc. London, **201**:133, 1910.

15. Dubois, D., and Dubois, E. F.: A Formula to Estimate the Approximate Surface Area if Height and Weight be Known, Arch. Int. Med. **17**:863 (June) 1916.

16. Keith, N. M.: The Total Circulating Volume of Blood and Plasma in Cases of Chronic Anemia and Leukemia, Am. J. M. Sc. **165**:174 (Feb.) 1923.

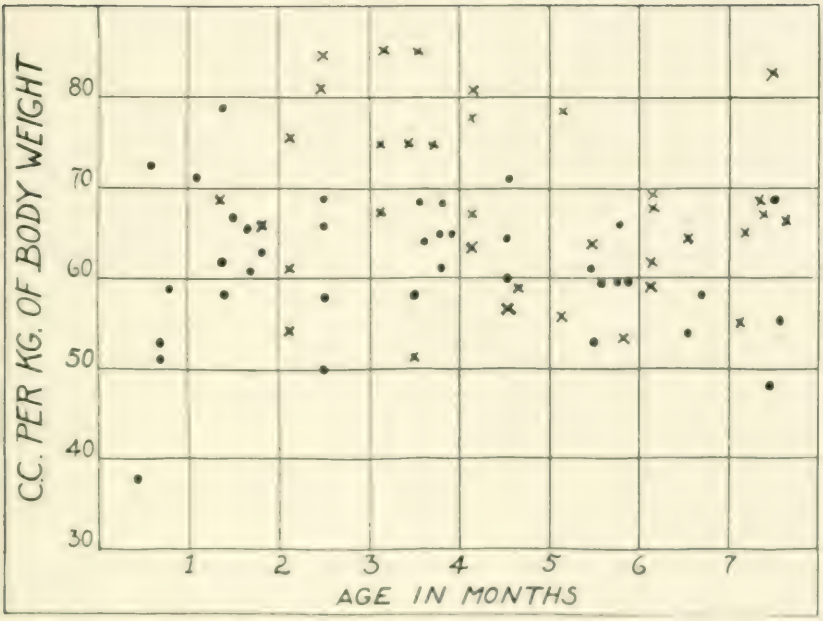

Chart 5.—The volume of plasma per kilogram of body weight in relation to age in infants with severe malnutrition.

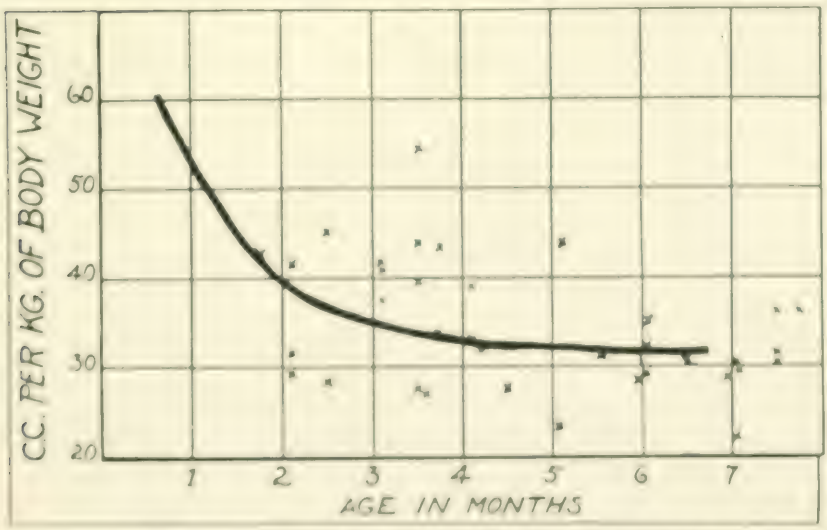

Chart 6.—The volume of red cells per kilogram of body weight in relation to age in infants with severe malnutrition.

The Relation Between the Serum Protein Per Cent. and the Plasma Volume.—No relation was found between the plasma volume per kilogram of body weight and the serum protein per cent.

SUMMARY AND CONCLUSIONS

1. A micromodification of the dye method of Keith, Rowntree, and Geraghty has been described, by which the volume of blood can be determined with 4 c.c. of blood.

2. At birth, the corpuscular volume is relatively high. It falls rapidly during the first weeks of life, so that the absolute volume of red cells is less at 8 weeks of age than at birth.

3. The volume of blood and plasma in infants is higher in relation to the body weight and varies more widely than in adults. The average value for the blood volume is 101 c.c. per kilogram of body wieght. The average value for the plasma volume is 61 c.c. per kilogram of body weight.

4. The volume of blood and plasma in marantic infants is higher than in normal infants.

5. The volume of blood per unit of body surface in infants is much smaller than in adults (1.7 liters per square meter for infants, 3.12 liters for adults).

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THE WATER CONTENT OF INFANTS' BLOOD DURING PERIODS OF RAPID INCREASE IN WEIGHT

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THE WATER CONTENT OF INFANTS' BLOOD DURING PERIODS OF RAPID INCREASE IN WEIGHT*

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These studies were undertaken in order to determine whether or not there is an increase in the water content of the blood during the rapid gains in weight which not infrequently occur in healthy, artificially fed infants. Freund [1] has shown that these large weight increases are due to water retention. He studied the nitrogen and chlorid balance in a series of artificially fed infants and found that during the days of rapid gain the nitrogen retention was sufficient to account for only a small part of the increase in weight. That the major part was due to water retention was shown by the marked diminution in the elimination of chlorid and alkali salts.

In these studies the refractometric method was used to determine variations in the blood water. The technic employed was similar to that described in previous papers.[2] The serum proteins were calculated from the refractive index of serum according to the formula of Reiss.[3]

Five babies were used in this study. The babies chosen were healthy in the sense that they were not suffering from acute illnesses. Some of them were slightly underweight. In most instances, the weight gains were induced by increasing the carbohydrate content of the feeding. Edema never occurred. The weighings were made by a nurse, specially assigned to the care of the babies. Blood determinations were made at frequent intervals before and after the weight gains.

REPORT OF CASES

Case I (Fig. 1).—S. W., a healthy boy, aged 3 months, was first observed Nov. 7, 1922, when he weighed 4,100 gm. His feedings consisted of 390 c.c. of whole milk, 45 gm. of lactose and 300 c.c. of barley water.

November 8 an increase in the feeding was instituted to 465 gm. A theory test or weight balance the baby gaining 450 gm. during the next seven days.

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* From the Pediatric Division of the New York Nursery and Child's Hospital, and the Department of Pediatrics, Cornell University Medical College.

1. Freund, W.: Wasser und Salze in Ihren Beziehungen zu den Körpergewichtsschwankungen des Säuglings, Jahrb. f. Kinderh. **59**: 425, 1904.

2. Barwin, Harry: Dehydration in the Newborn, Am. J. Dis. Child. **24**: 497 (Dec.), 1922.

3. Reiss, E.: Der refraktometrische Eiweissstoffwechsel und dessen Ergebnisse für die Physiologie und Pathologie des Menschen, Ergebn. d. inn. Med. u. Kinderh. **10**: 343, 1913.

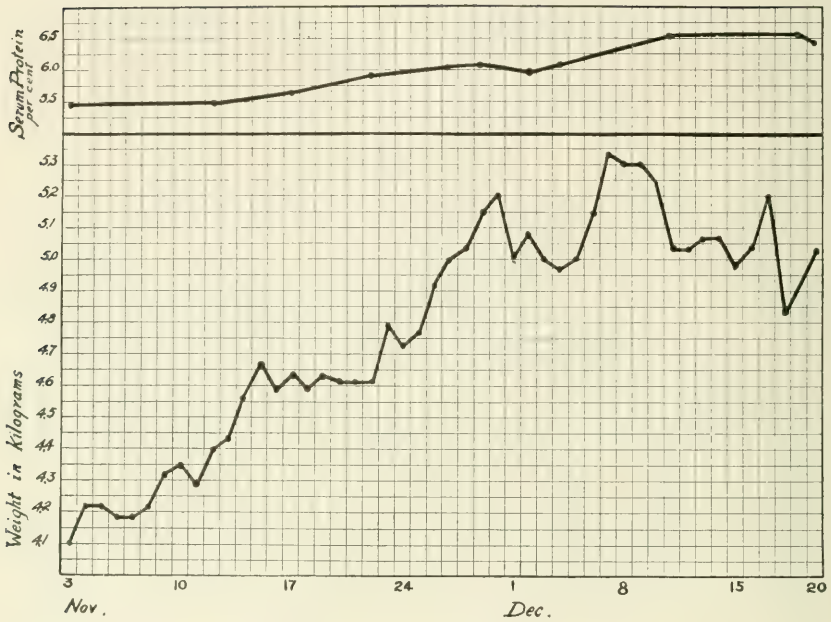

Chart 1.—Findings in Case 1.

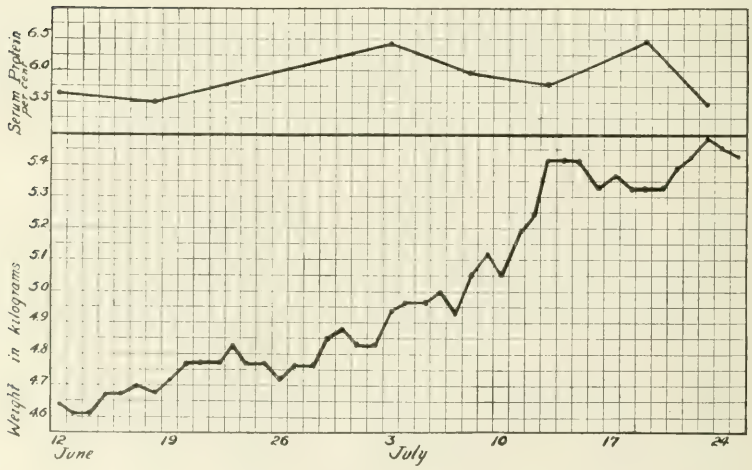

Chart 2.—Findings in Case 2.

an average daily gain of 65 gm. The weight remained stationary after this, and, November 19, the lactose was further increased to 150 gm., the amount of milk and water in the formula remaining unchanged. There was a slight gain in weight.

November 24, 180 gm. of maltose were substituted for the lactose in the feeding. This was followed by a sharp rise in weight so that the baby gained 470 gm. between the twenty-fourth and the thirtieth of November, an average daily gain of 79 gm. During this period the stools were frequent and slightly watery. December 1, the maltose was omitted from the feeding. The weight remained stationary, and the stools diminished in number and improved in consistency.

December 4, 180 gm. of maltose were again added to the feeding. Again a sharp rise in weight occurred, the baby gaining 360 gm. in three days. The maltose was again omitted from the feeding. The baby lost weight sharply. December 12, 30 gm. of maltose were added to the feeding, and, December 16

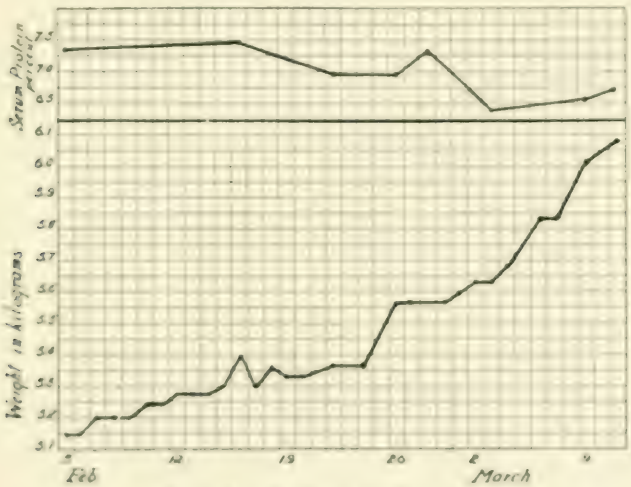

Chart 1.—Findings in Case 1.

this was increased to 45 gm. The second increase in the diet was followed by a sharp rise and then by a fall in weight.

Despite the marked variations in the weight, the serum proteins were little affected. They rose slowly and regularly from 5.81 November 2 to 6.31 per cent., December 21.

Case 2 (Fig. 2).—H. L., a healthy boy, aged 2½ months, was first observed, June 13, 1920, when he weighed 4640 gm. He was receiving a feeding containing of 420 c.c. of whole milk, 60 gm. of dextrinmaltose and 450 c.c. of barley water, on which he gained slowly.

June 6, the dextrinmaltose in the feeding was increased to 75 gm. and, June 9, to 90 gm. Following the second increase, there was a sharp rise in the weight, the baby gaining 370 gm. in three days. Coincident with the rapid gain in weight, there was a slight fall in the serum proteins from 5.9 per cent. July 8, when the weight was 5050 gm. to 5.6, July 13, when the weight was 5430 gm. The fall in serum protein concentration was only slightly greater than could be accounted for by errors inherent in the method for the collection and examination of the blood specimens.

Case 3 (Fig. 3).—A. G., a healthy boy, aged 3 months, was admitted, Jan. 24, 1920, when he weighed 5400 gm. He had been under treatment for congenital

syphilis in the outpatient department since birth, but he showed no active lesions during his stay in the hospital. The blood Wassermann reaction was negative.

The infant was given a feeding consisting of 660 c.c. of whole milk, 60 gm. of lactose, and 240 c.c. of barley water, on which he gained slowly. Feb. 25, 1920, the lactose in the feeding was increased to 75 gm. Between February 24 and February 26, the baby gained 200 gm. During the marked increase in weight the serum protein precentage remained unchanged, indicating that the plasma water was not increased. On March 4, the lactose in the

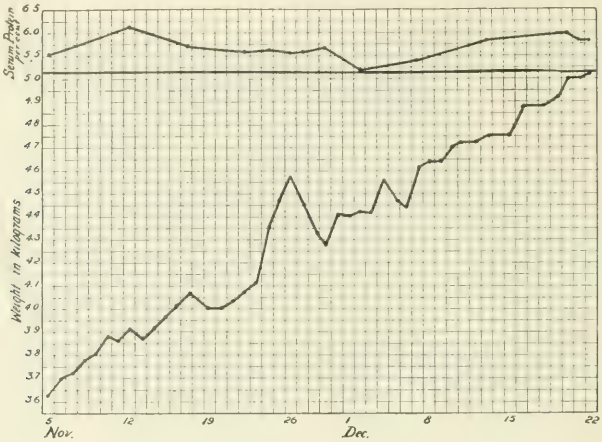

Chart 4.—Findings in Case 4.

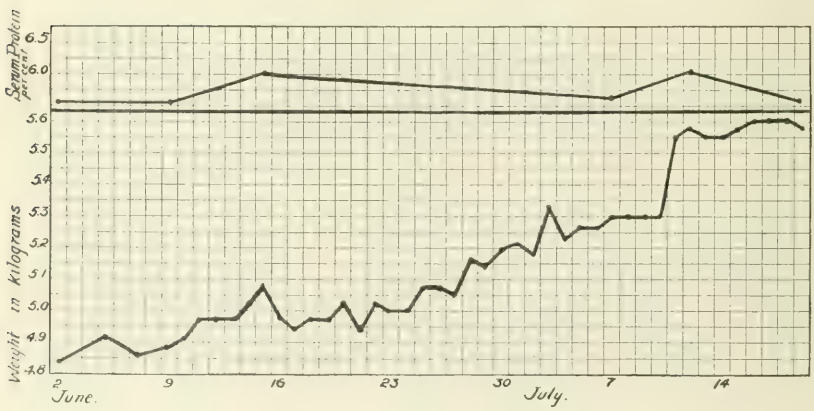

Chart 5.—Findings in Case 5.

feeding was further increased to 105 gm. During the following six days, the baby gained 380 gm., an average daily gain of 63 gm. Here again there was no fall in the serum protein concentration during or after the periods of rapid weight gain.

Case 4 (Fig. 4).—H. M., a healthy boy, aged 2 months, was first observed, Nov. 5, 1920, when he weighed 3,630 gm. He was receiving a feeding consisting of 360 c.c. of whole milk, 90 gm. of lactose and 360 c.c. of water, on which he gained well. November 20, the milk in the feeding was increased to 450 c.c.

November 23, 100 gm. of maltose were substituted for the 90 gm. of lactose in the feeding. During the next three days the baby gained 470 gm., and in the following three days he lost 300 gm. During the period of rapid gain and loss, the serum protein concentration remained unchanged.

Case 5 (Fig. 5).—F. B., a healthy boy, aged 4 weeks, was admitted, April 9, 1920, when he weighed 3,970 gm.

June 2, when observations were started, he weighed 4,840 gm. and was receiving a feeding consisting of 420 c.c. of whole milk, 90 gm. of lactose and 390 c.c. of barley water, on which he gained slowly. June 19, the feeding was changed to 420 c.c. of whole lactic acid milk, 105 gm. of dextrimaltose and 390 c.c. of barley water. He did well on this until July 10, when, without change of feeding, he gained 250 gm. within twenty-four hours. During this twenty-four hour period he passed only 33 c.c. of urine.

Despite the marked gain in weight, no significant change in the serum protein concentration occurred, indicating that there was no increase in the water content of the plasma.

Comment

The effect of rapid gains in weight on the blood water was studied refractometrically in five cases. In no instance did a significant increase in the blood water occur. Since the increase in weight represents an increase in the water content of the organism, it seems clear that the increased amount of fluid is held in the tissues.

Summary and Conclusions

1. Freund has shown that marked variations in the weight curve of an artificially fed infant are due to changes in the water content of the organism.

2. Variations in the blood water were studied with the refractometric method in five babies before and after marked increases in weight.

3. Despite marked gains in weight (presumably due to an increase in the water content of the organism), no significant increase in the water content of the plasma occurred.

4. An increase in the amount of tissue fluid may occur in the healthy, artificially fed infant without a corresponding increase in the water content of the plasma.

THE LEUKOCYTE COUNT IN THE NEW-BORN WITH DEHYDRATION FEVER*

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NEW YORK

The purpose of these observations was to determine whether or not an increase in the leukocyte count accompanies the transient fever which frequently occurs in the new-born during the first week of life. It has long been thought that this fever may be due to dehydration. Holt,[1] in 1895, pointed out that it occurred in infants who had lost a great deal of weight (a part of which, presumably, is due to water loss), and that it could be cured by the administration of fluids. In a recent paper,[2] it was shown that the transient fever of the new-born is associated with a decrease in the plasma water, as indicated by an increase in the protein concentration of serum, determined refractometrically. The oral administration of warm water results in a drop in the temperature to normal within from thirty to ninety minutes. This is accompanied by an increase in the water content of the blood, as shown by a fall in the serum protein concentration and the red cell count.[3] In infants with fever due to infections, the serum proteins are not increased, and no significant fall in temperature follows water gavage despite the fact that this procedure is followed by an increase in the blood water.

Bacon, Notty, and Rapley[4] in a study of the leukocyte count in dehydration fever in animals, induced fever by rapidly injecting hypertonic salt solutions into the femoral vein of dogs after the manner described by Bakwin, Sampson and Woodyatt.[5] At the end of the first hour, they found a slight leukopenia with a relative increase of the small lymphocytes. Following this there was a steady rise in the leukocyte count to levels far above normal. The increase was almost wholly confined to the polymorphonuclear leukocytes.

* From the Pediatric Division of the New York Nursery and Child's Hospital, and the Department of Pediatrics, Cornell University Medical College.

1. Holt, L. E.: Diarrhœa Fever in the Newly Born, Arch. Pediat. **12**: 240, 1895.

2. Bakwin, Harry: Dehydration Fever in the New-Born, Am. J. Dis. Child. **24**: 501 (Dec.) 1922.

3. Bakwin, Harry; Morris, R. M., and Sampson, J. D.: To be published.

4. Bacon, D. R.; Notty, F. S., and Rapley, H. H.: Factors in Leukocytosis, Arch. Int. Med. **30**: 259 (Aug.) 1922.

5. Bakwin, J. G.; Sampson, W. H., and Woodyatt, R. T.: Fever and Water Reserve of the Body, Arch. Int. Med. **24**: 116 (July) 1919.

Bacon and his co-workers point out the similarity in the leukocytic reaction in experimentally produced dehydration fever and in the fever following the injection of a foreign protein. They believe that the mechanism by which fever and leukocytosis are produced is identical in both conditions. According to them, the acute water shortage in

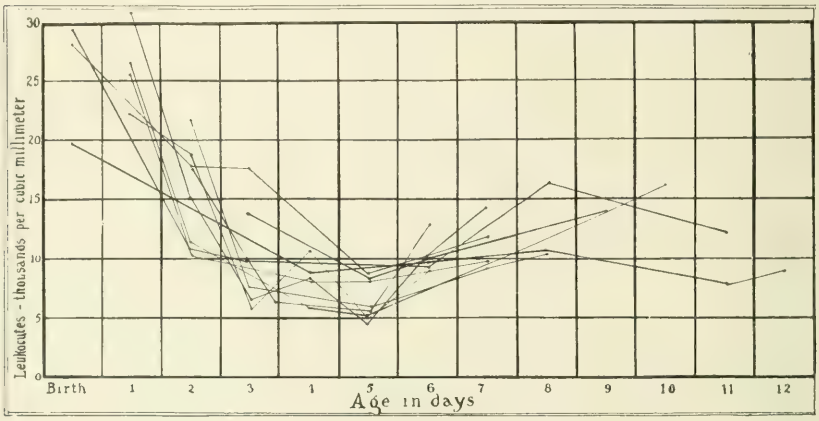

Chart 1.—Variations in the leukocyte count of afebrile new-born infants during the first few days of life.

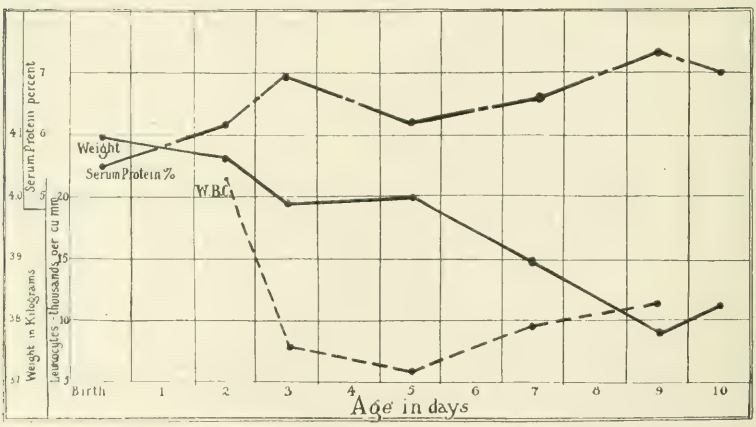

Chart 2.—The lack of relationship between variations in blood concentration and the leukocyte count is shown. As the weight falls, the percentage of serum protein rises, indicating a diminution in the plasma water. The increase in weight is accompanied by a return of the serum proteins to normal. The physiologic drop in number of the leukocytes occurs during the first five days, despite the increase in blood concentration.

dehydration fever results in an accelerated protein metabolism with the greater productions of its by-products, such as urea and creatinin. As evidence for this hypothesis, they point to the rise in the nonprotein

nitrogenous constituents of the blood that occurred regularly in their dogs with dehydration fever.

Rietschel [6] has recently called attention to a nonbacterial form of fever which he calls "dynamisches Eiweissfieber." He produced it in infants by feeding concentrated diets of high protein content, and

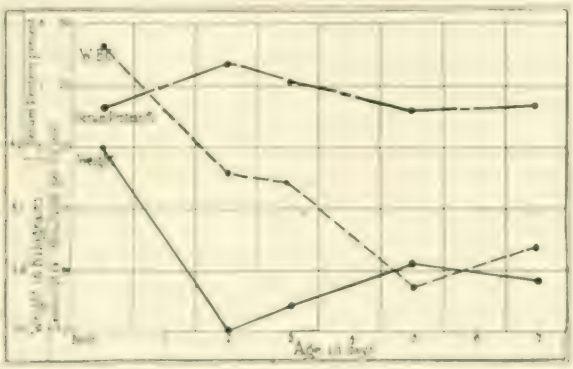

Chart 4.—The lack of relationship between variations in blood concentration and the leukocyte count is shown. The fall in leukocytes during the first week and the slight rise during the second week are entirely independant of the blood concentration, as measured by variations in the percentage of serum protein.

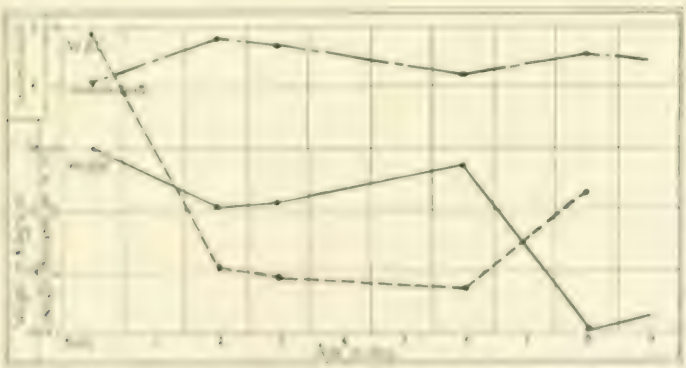

Chart 4.—The lack of relationship between variations in blood concentration and the leukocyte count is shown. The fall in the number of leukocytes during the first week and the slight rise during the second week are entirely independent of the blood concentration, as measured by changes in the percentage of serum protein.

he ascribes it to the abnormal metabolism resulting from the high specific dynamic action of protein. Because of the low fluid content of the diet, sufficient water is not available for the elimination of the

6 Rietschel: Dynamisches Eiweissfieber, Klin. Wchnschr. 2: 9 (Jan. 1) 1923

increased amount of heat from the body surface by evaporation. (Somewhat similar examples of fever of nonbacterial origin in infants have been described by Finkelstein,[7] Holt and Levene [8] and Benjamin.[9])

No figures are available concerning the leukocyte count in new-born infants with dehydration fever. Repeated determinations were made on a large series of infants during the first ten days of life. Blood was obtained from the toe from three to four hours after a feeding, and counts were made in the usual manner. Blood for serum protein concentration was collected at the same time. The technic employed was similar to that described in previous papers.[10] The temperature was taken at the time of puncture.

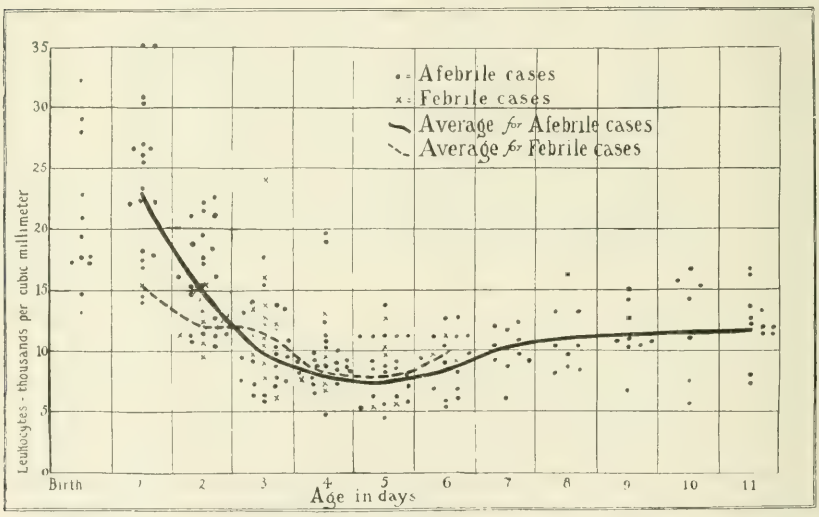

Chart 5.—The leukocyte count in afebrile and febrile new-born infants. The average curves are almost identical.

Because of the wide variations in the number of leukocytes during the first weeks of life, a group of afebrile babies was studied. Our results correspond fairly closely to those of previous observers.[11] On the first day (Table 1 and Chart 1), the white cells are markedly

7. Finkelstein, H.: Ueber alimentärisches Fieber, Deutsch. med. Wchnschr. **35**:190, 1909.

8. Holt, L. E., and Levene, P. A.: The Influence of High Protein Feeding on the General Metabolism, on the Intestinal Flora, and on the Body Temperature of Infants, Am. J. Dis. Child. **4**:265 (Nov.) 1912.

9. Benjamin: Weitere Untersuchungen zum Eiweissnährschäden des Säuglings, Jahrb. f. Kinderh. **80**:545, 1914.

10. Bakwin, Harry: Dehydration in the New-Born, Am. J. Dis. Child. **24**:497 (Dec.) 1922.

11. Von Reuss, A. R.: Diseases of the New-Born, London, 1921, p. 42.

increased in number, usually ranging between 20,000 and 25,000 per cubic millimeter. They fall rapidly and reach the adult level on the fifth to the seventh day. A rise to 10,000 or 12,000 follows, during the second week.

It has been suggested that the leukocytosis in the new-born is due to an increase in the blood concentration. Repeated simultaneous observations on the white cell count and the serum protein concentration show that the variations in the leukocytes are entirely independant of

Table 1.—Daily Variations in the Leukocyte Counts in Afebrile and Febrile New-Born Infants

	Afebrile				Febrile			
Age, Days	Number of Cases	Leukocytes per C. Mm. Maximum	Minimum	Average	Number of Cases	Leukocytes per C. Mm. Maximum	Minimum	Average
Birth	77	22,400	17,200	20,000	0			
1	59	23,400	16,800	22,400	7	15,400	12,400	13,400
2	63	22,000	15,400	18,000	7	14,400	9,800	12,200
3	53	17,700	13,500	15,000	15	14,000	6,000	11,500
4	72	14,000	4,800	9,200	9	13,000	6,600	8,500
5	61	13,500	5,400	7,800	6	12,200	5,400	8,500
6	53	12,400	5,200	8,800	5	11,200	9,400	10,100
7	39	11,100	7,400	10,000				
8	9	12,200	8,000	10,600				
9	8	13,000	6,400	10,800				
10	7	12,000	5,200	9,100				
11	11	11,400	7,200	9,200				
12	8	12,400	9,100	9,400				

Table 2. Temperature and the Leukocyte Count in Newborn Infants

Temperature		Number of Cases	Leukocytes per C. Mm. Maximum	Minimum	Average
Centigrade	Fahrenheit				
36.2	97	11	20,000	4,800	10,800
36.4	98	140	22,400	5,400	11,000
36.6	98	91	20,200	7,000	11,200
36.8	98	70	14,000	5,200	11,000
37.0	99	37	14,400	8,200	11,400
37.2	99	20	12,400	8,000	11,000
37.4	99	9	20,000	7,200	11,200

changes in the blood concentration determined nitrogenometrically (Charts 2, 3 and 4).

The daily leukocyte counts in new-born infants with and without fever are presented in Table 1. It will be seen that the daily variations in the white cell counts of babies with fever corresponds closely to the variations of those without fever. This is graphically represented in Chart 5.

In Table 2, the leukocyte counts are arranged according to the temperatures. No relationship was found between the degree of fever and the leukocyte count.

SUMMARY AND CONCLUSIONS

1. At birth, the leukocytes are increased, the counts usually ranging between 20,000 and 25,000 per cubic millimeter.

2. There is a rapid fall to normal during the first week, followed by a rise, usually starting on the fifth day, to from 10,000 to 12,000.

3. The variations in the leukocyte count are not due to changes in the blood concentration.

4. There is no change in the leukocyte count in new-born infants with dehydration fever, the daily average in those with fever corresponding closely to that in babies without fever.

We wish to express our indebtedness to Dr. H. M. Painter for the use of material from the obstetric service of the New York Nursery and Child's Hospital.

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CONGENITAL DIAPHRAGMATIC HERNIA OF THE RIGHT SIDE; ITS DIAGNOSIS IN LIFE.*

By Philip Moen Stimson, M.D.
New York.

Introduction. Hernias through the diaphragm can no longer be classed as rarities. As far back as 1911, Eppinger[1] tabulated 635 cases of diaphragmatic hernia of all types, collecting them from the medical literature of numerous countries. Of these cases, 580 were left-sided, and only 55 right-sided; that is, he found records of over ten hernias into the left chest for each hernia into the right chest. Four years later, a rather extensive classified review by Kienboeck[2] of the German literature alone up to 1915, revealed only three diaphragmatic hernias of all types and one eventration as having been diagnosed in life and confirmed at autopsy.

In recent years, however, the x-ray has allowed many cases of this interesting condition to be diagnosed before the patients reached the operating or autopsy tables, and many additions have been made to the knowledge of the subject. However, hernias through the right side of the diaphragm have continued rarities, and a fairly extensive search of the literature has revealed references to only four such cases that have been diagnosed in life. The opportunity to observe a fifth such case, the youngest of the group, has been the inspiration of the present paper.

Anatomy. The diaphragm is a partition between the abdomen and the thoracic cavities, which is composed of three layers, an upper covering of pleura, a muscle layer, and a lower layer of peritoneum. The muscle layer is composed of contiguous groups of muscle fibres which radiate in from the chest wall to a central fibrinous tendon which is slightly greater in area on the left side than on the right. The groups of muscles are sometimes named from their peripheral attachments, the pars sternalis, the pars costalis right and left, and the pars vertebralis. There are two natural openings through the diaphragm, that of the oesophagus through the muscle fibres slightly anterior and to the left of the spine; and that of the inferior vena cava through the tendinous part of the diaphragm about midway from sternum to spine and slightly to the right of the midline. The descending

* Read before the Clinical Research Society, April 3, 1923, and before the American Pediatric Society, May 10, 1923.
From the Department of Pediatrics, Cornell University Medical College.

aorta passes down behind the diaphragm rather than through it.

In the embryo, the diaphragm largely originates in the neck in the septum transversum, the sternal or anterior part of which gives origin to the pars costalis and pars sternalis, while a dorsal part gives rise to the pars vertebralis. As the forming partition moves down across the future chest, pulling the phrenic nerve with it, it allows the rudimentary lungs to pass through posterior openings between the pars vertebralis and the pars costalis on each side, and in the ordinary course of events, at about the end of the second month of gestation, these openings in the diaphragm, situated one on each side of the spine and sometimes called the

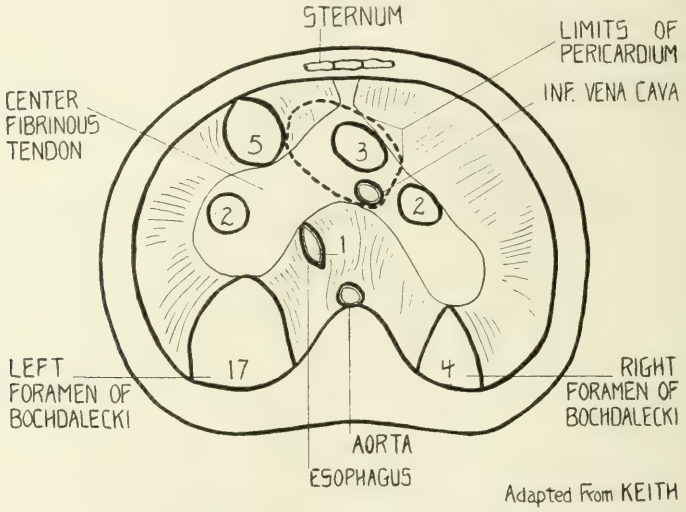


FIG. 1. Keith's diagram of a diaphragm showing the anatomical relationships, and the locations of the 34 hernias of his series.

foramina of Bochdalecki, close up, the one on the right side usually closing first. But even as in the internal abdominal rings, the internal openings of the tunica vaginalis may be delayed in closing or fail to close altogether, so here also in the diaphragm, defects may occur. On the right side, the liver growing in the septum transversum seems to guard to a considerable extent the right side of the diaphragm from developmental disturbances. Certainly, after birth, it protects weak spots in the diaphragm from giving way to sudden shocks which might cause herniation through similar spots in the left side where there is no protecting liver. Also, the formation of the left side is more complex than that of the right since it grows in close association with the left lobe of the liver, the stomach, the pericardial formation, one

of the pulmonary ridges, and the pleuroperitoneal membrane. Accordingly, we can expect to find congenital diaphragmatic hernias occurring usually through the posterior parts of the diaphragm and particularly on the left side, and such seems to be the case.

In 1910, Keith[1] reported an anatomic study of 34 specimens of diaphragmatic hernia then found in the medical museums of London. (Fig. 1.) Seventeen, or one-half of the entire number, were through the unclosed left foramen of Bochdalecki, and four were through the right. There was one through the esophageal opening. In two infants, congenital hernias were found through the left part of the central tendon, while through the right part of this tendon were two more hernias, but these latter were both of liver tissue and due to abnormal development of liver in the septum transversum. Further anteriorly, there were three hernias into the pericardium, two in adults and possibly traumatic in origin; the other in an infant that died at birth. And finally, through the muscle tissue of the left anterior part of the diaphragm, there were five cases, all in adults and all probably traumatic in origin.

Inasmuch as the paper is primarily concerned with hernias through the right foramen of Bochdalecki, it is interesting to note that of Keith's four such cases, two had died at birth, one had lived one and a half hours, and one four hours.

Diaphragmatic hernias are acquired or congenital; true or false. Eppinger[2] regards as acquired only those in which there is a definite history of a traumatism (such as a fall, a crushing accident, a penetrating wound, and the like) and he classes all others as congenital. The latter arise through embryological defects of the diaphragm, such as arrested development of a portion as already mentioned, excessive size of the natural foramina, or weakness of a part of the muscle layer.

A true diaphragmatic hernia is one where there is a sac of peritoneum and pleura around the herniating viscus, the muscle layer only being deficient, whereas in cases of false hernia there is a complete defect of the three layers of the diaphragm, and the abdominal organs, without a sac, pass directly into the pleural cavity, pericardium, or mediastinum. Owing to the negative pressure within the chest and the positive abdominal pressure, we find the abdominal organs passing into the chest rather than the thoracic organs into the abdomen. An associated condition is known as insufficiency or eventration of the diaphragm, where

in there is a thinning and ballooning upward of an entire half of the diaphragm with symptoms and signs often similar to those of diaphragmatic hernia.

CASES. Of cases of diaphragmatic hernia through the right posterior portion of the diaphragm that were diagnosed in life, I have found reference in medical literature to four, and I have a fifth such case, the youngest of all, to report.

CASE I. In 1910, Dietlen and Knierim[4] reported the diagnosis in life of a right posterior diaphragmatic hernia in a well-nourished 23 year old woman, mother of a healthy child, and pregnant a second time. Her symptoms of pain in the right chest had dated from her sixteenth year. Solid foods had given severe symptoms of distress, but fluids gave little or no pain. The pain, when present, was usually in the pit of the stomach, but sometimes

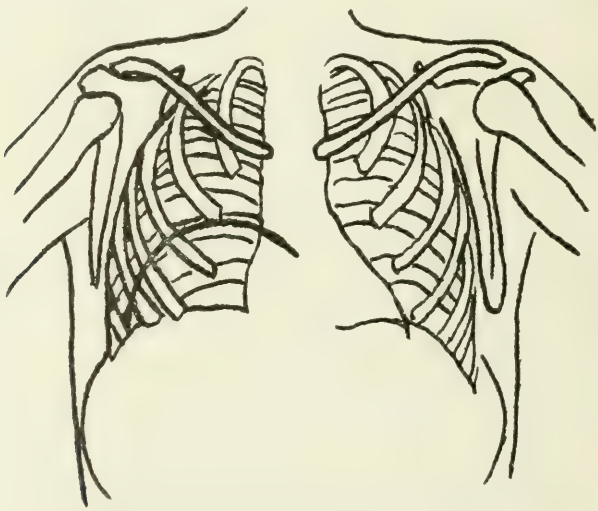


FIG. 2. The "curved line" found by Dietlen and Knierim.

radiated towards the right breast or was marked beneath the right shoulder blade. She had vomited some blood before admission to the hospital.

The first findings suggested a pleural exudate but were not typical. A simple x-ray showed an arched line curving above the right side of the diaphragm (Fig. 2) and a subdiaphragmatic abscess was suspected, especially after an exploratory puncture yielded a cloudy, bright-yellow fluid containing numerous pus cells. Subsequent x-rays with bismuth revealed, however, as shown in their diagrams, that part of the stomach passed through the diaphragm.

The authors stated that since there were no reasons to consider the case traumatic in origin, it was probably developmental or congenital in type. They considered their case unique as no cases of right-sided diaphragmatic hernia, diagnosed in life, had been described up till then. Their paper makes no mention of the treatment or outcome of the case.

CASE II. In Holt's text-book, edition of 1917,[5] are reproduced two x-ray plates which show the stomach in the right side of the chest of a child 16 months old, who later died of pneumonia at 3½ years.*

CASE III. In 1919, DeCourcy[6] reported the case of a 25 year old girl who had given a history of at least eight years of constipation and indigestion, and of more recent severe epigastric pains immediately after meals. There had also been marked vomiting without premonition, the vomitus seeming to gush from the patient. It was also stated that there was smothering and shortness of breath at times, which is of especial note since similar respiratory symptoms are not recorded for any of the other patients of this little series. The diagnosis here was made by a prolonged fluoroscopy of a test meal, the stomach being found at first to be partly in the right chest, but in a half hour it was entirely in the abdomen.

The patient was operated upon, the stomach pulled down, and a purse string suture made around the diaphragmatic opening.

CASE IV. This case, a truly remarkable one, was reported in 1920 by Keith.[7] A 17 year old boy gave a history beginning at 18 months (when he was very robust and weighed 23 pounds) of a prolonged attack of persistent vomiting and rapid loss of weight to seven or eight pounds in two months. Then there was freedom from symptoms for six months and a return to health, and subsequent similar ups and downs until the age of 17 was reached, the longest period without symptoms being two years.

In a fluoroscope, at first only the pyloric end of the stomach showed in the right side of the chest, but three weeks later the whole stomach seemed to be in the chest. Accordingly, the patient was operated upon, and the entire stomach was found in the right chest having passed through a lateral slit in the diaphragm, to the right of the spinal column. The opening was approximately 1½ by 2½ inches. The stomach was pulled out of the chest in this operation and two weeks later the diaphragmatic open-

* Same cases as the one cited in Case [illegible] from [illegible].

ing was closed by the transthoracic route. Recovery was uneventful resulting in a complete cure. Subsequent fluoroscopy and x-ray plates showed no filling defects in the esophagus, stomach, or cap, but a moderate dilatation of the stomach and ptosis of about two inches.

CASE V. AUTHOR'S CASE—PRELIMINARY REPORT. Edwin F. was brought to the Cornell Pay Clinic on August 11, 1922, when exactly 11 months old, the complaints in his behalf being almost continuous vomiting since the third day of life and the resulting severe malnutrition. He was born September 11, 1921, of healthy parents, it having been his mother's first pregnancy.

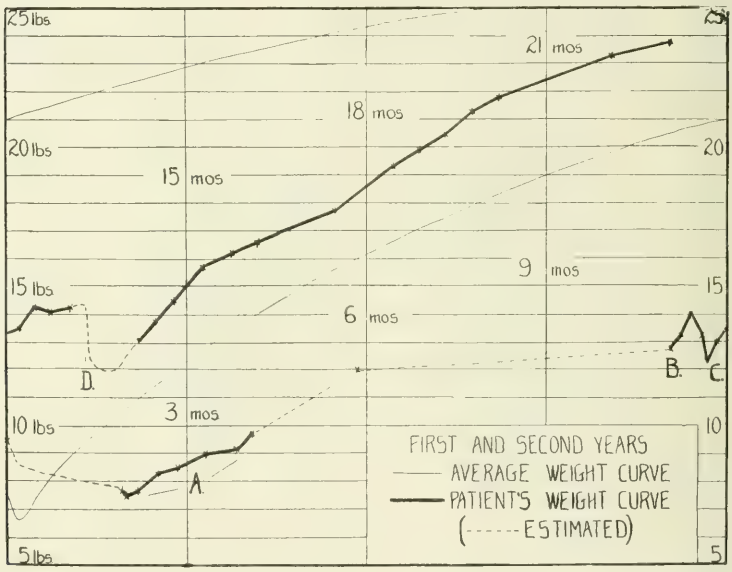


FIG. 3. Author's case. Weight curve. A. Section of curve reconstructed from outside records. B. When the patient was first seen. C. When the diagnosis was discovered. D. When the patient was taken to the hospital for four days.

He was a full term, 9½ pound baby, born without instruments and seeming to be perfectly formed and normal in every respect. There was no cyanosis nor notable difficulty in breathing the first day, nor has there been either since. He was nursed nearly two months but since he had vomited from two to all feedings a day after the third or fourth day, he was tried on condensed milk. This failing to help, he was taken to one of New York's noted specialists who found nothing abnormal at that time in a physical examination other than malnutrition, and put him on a malt soup mixture on which the boy gained quite

well (Fig. 3). He continued to vomit considerably but possibly not so much as formerly. Later, other doctors were consulted, and the baby was tried on buttermilk, whey, and various combinations of milk. Curiously enough, on each new feeding he usually did well for from four to seven days but then began vomiting frequently and quickly lost what weight he had gained. His bowels were almost always constipated except during the short period he was on condensed milk, but his mother usually accomplished satisfactory results with milk of magnesia. He had had what was considered bronchitis in March, and also had been subject to boils on his forehead, especially when most upset. Otherwise, he had had no illnesses but seemed to be a definite case of marasmus when first seen at 11 months.

At this time, August 11, 1922, he weighed only 12 pounds, 13 ounces, and a routine physical examination revealed nothing abnormal except the marked malnutrition and the absence of teeth and of the ability to creep or stand. He cried violently most of the time. He was put on a thick cereal formula of skimmed milk boiled with farina and milk sugar on which he gained 12 ounces in 12 days during which period there was no vomiting at all. But then he began vomiting moderately so that he lost 4 ounces in seven days. At this point the vomiting became very severe, nothing whatever being retained, and he lost 16 ounces in the two days preceding September 1st.

Accordingly, that morning in the clinic, an attempt was made at 10:30 to wash out his stomach but no milk was obtained. He had been given a bottle at 10:00 and there had been profuse vomiting at 10:15. It was noticed that in passing the catheter down his esophagus, there seemed to be some difficulty in entering the stomach, and accordingly it was thought that there might be some obstruction at the cardia—at least a cardiospasm. A catheter full of a barium preparation was then passed and more barium introduced. It was observed that the barium was immediately vomited until the catheter end had seemed to pass the obstruction after which time the vomiting ceased. With the aid of Dr. H. H. Fellows, the child was then quickly fluoroscoped, and the stomach was found on the right side, apparently on a level with the liver and possibly behind it. A sharp angulation at the cardia was made out with a little barium still in the lower end of the esophagus just above this constriction. Because of the child's exhausted condition, only a short examination could be made but x-ray prints were taken. These later proved unsatisfactory so

that on September 5, four days later, the child being appreciably stronger, new x-ray prints were taken with a catheter passed into the stomach and then filled with barium.

In these pictures (Figs. 4 and 5), the heart and liver were found apparently in their normal positions, and so also the pyloric and cardiac ends of the stomach. But the greater curvature of

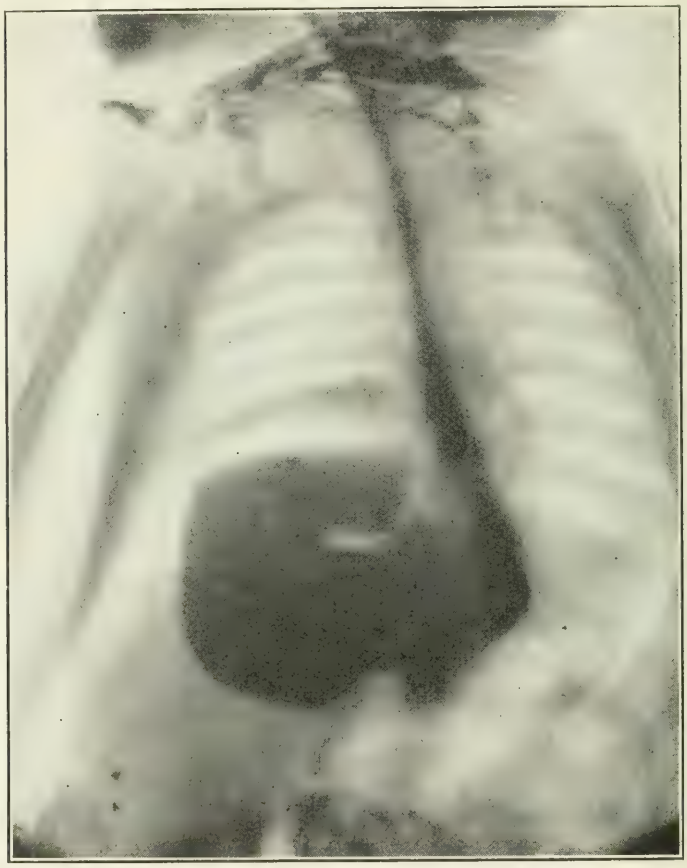
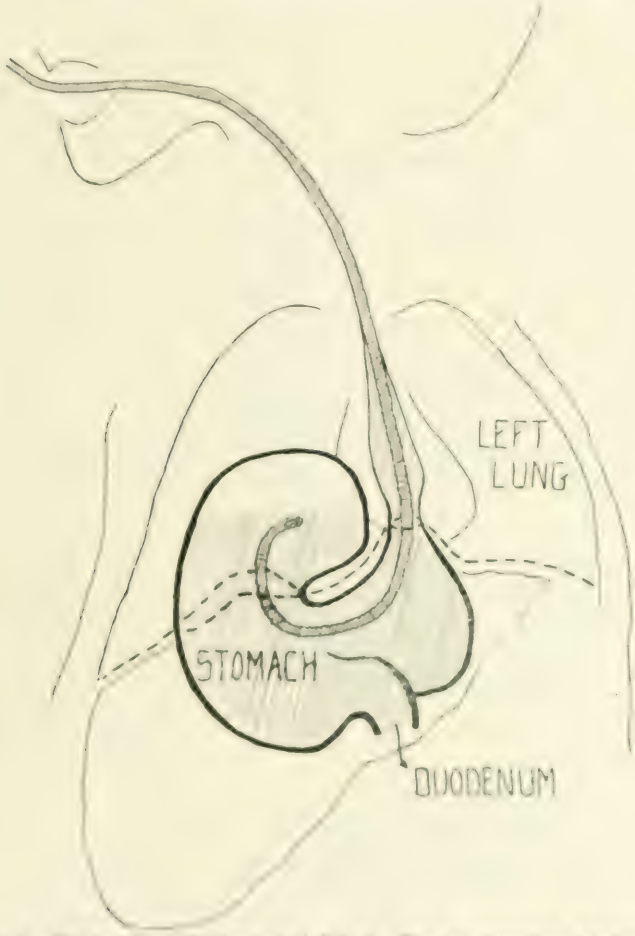


FIG. 4. Author's case. The x-ray picture which gave the diagnosis. (See Fig. 5.)

the stomach had been pulled over to the right and some of the wall had been sucked up into the right chest cavity. Six weeks later, on October 13, a fluoroscopic examination showed the entire stomach in the chest (Fig. 6), but there was apparently no obstruction to its emptying. In fact, it seemed to empty itself of the barium unusually rapidly and this was also noted in the previous examinations.

By giving small feedings slowly and at frequent intervals, some progress in weight was made in September and October but on October 19 violent vomiting commenced, at first only of all food, but a day later of a brownish-black fluid considered digested blood by several doctors. On October 21, he was admitted to the



New York Hospital with a temperature of 102.4°, which rose in two days to 106°, apparently due to a complicating bronchitis. The vomiting became less marked and on the 24th he was fluoroscoped by Dr. A. L. Holland who made the following notation: "The entire stomach is found above the diaphragm. The cardia seems constricted. The duodenum seems also within the chest

and leaves in quite near the place where the cardia enters. The hernial opening is near the spine just to the right of it. No pyloric obstruction; apparent constriction at the cardia."

The child was shortly taken home from the hospital by the parents without an operation, and in November was brought back

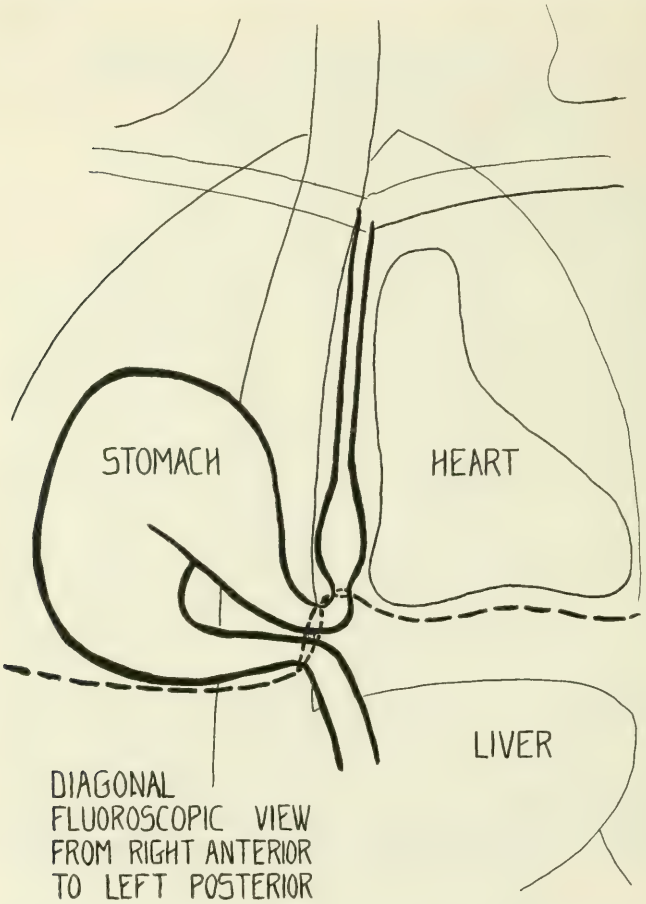


FIG. 6. Author's case. Diagram showing the fluoroscopic findings of Oct. 13th and 24th. The diagonal view was made to outline the esophagus between the shadows of the heart and spine. The obstruction at the lower end of the esophagus appears clearly, as well as the position of the stomach in the right side of the chest.

to the Cornell Clinic. At this time, the baby still weighed only 13 pounds, just what he had weighed in August. This day only was it first possible to note in any satisfactory manner the physical signs of the child's chest because usually he cried a great deal. There seemed to be some dullness at the right base posteriorly

with diminished breath and voice sounds, and at the left base there was some hyperresonance. X-ray films of the chest were taken without barium, and showed the presence of gas above the liver in the right side of the chest. (Figs. 7 and 8.)

Since this time there has been a steady and satisfactory gain in weight. (Fig. 3.) In November and December he vomited occasionally but since then there has been practically no vomiting. The diet has been the usual one for the second year, viz. cooked cereals, green vegetables, potato, broths, milk, toast, and orange juice, with also a little cod-liver oil, but everything has been given very slowly and in small quantities at a time, and the child has been held at least semi-erect during the feedings. At first there were a number of small meals a day, but at 24 months the child has three good sized meals only, has 16 teeth, walks, says many words clearly, and weighs 25 pounds, 1 ounce.

At no time has there been any cyanosis or dyspnea, nor other respiratory symptoms except during the two so-called attacks of bronchitis. Nor have any abnormal physical signs been made out at any time other than those already noted and the absence of marked gastric tympani under the left lower ribs, and even this usually seems present presumably due to a distended large intestine.

The present plan is to continue the expectant method of treatment until the little patient is four or five years old when, if he seems to be a fairly good surgical risk and if x-rays show the stomach is still in the right chest, operation may be urged.

SYMPTOMS. The usual symptoms described in cases of congenital diaphragmatic hernia are cyanosis, rapid respiration, a sunken abdomen, an over distended chest, and dyspnea, all these appearing very soon after birth. In those who survive longer, dyspnea is generally the most prominent symptom. It may be constant; it may occur in severe paroxysms, and there may be attacks of cyanosis often of great severity, these being produced by an accumulation of gas in the herniated hollow viscus. Davis[7] has recently reported a case of left-sided diaphragmatic hernia in an infant that showed intense cyanosis when prone but very marked improvement when held erect. Her little patient did well for several months when held fastened to a board kept elevated at an angle of over 45 degrees.

In discussing 127 cases of diaphragmatic hernia of all types which he had assembled from the literature, Lane[8] stated that in all cases in which death was the direct result of the diaphragmatic

defect, cyanosis accompanied by extreme dyspnea, and vomiting were characteristic symptoms. Vomiting is usually spoken of as among the symptoms but apparently as secondary in importance to the respiratory symptoms, but Holt[3] says that the symptoms may at times suggest intestinal obstruction.

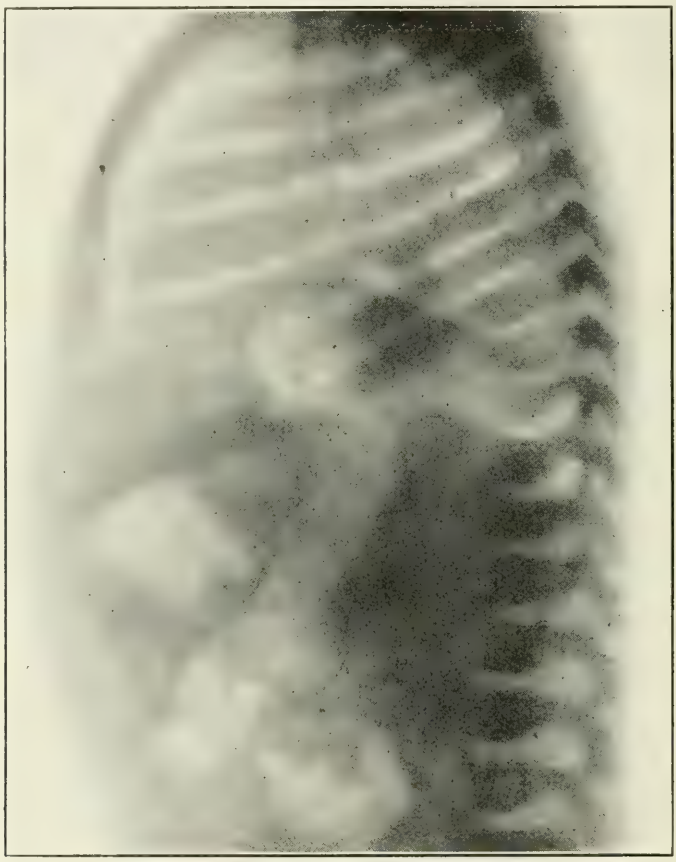


FIG. 7. Author's case. Lateral view (without bismuth) showing gas shadows; above the liver; through the liver shadow; and also apparently at the normal site of the stomach.

In the little series of right-sided hernias described in this paper, it is interesting to note that respiratory symptoms were noted in only one of the four cases where there is information as to the symptoms. But in all four instances, marked persistent vomiting was present, profuse vomiting, often projectile, and repeated so frequently as profoundly to affect the nutrition. The two women also complained of severe pain, in the one case de-

scribed as epigastric; in the other as radiating into the right breast or under the right shoulder blade.

PHYSICAL SIGNS. The physical signs elicited in cases of diaphragmatic hernia naturally depend upon the size and location of the hernia, and the nature of the herniating viscus. In cases

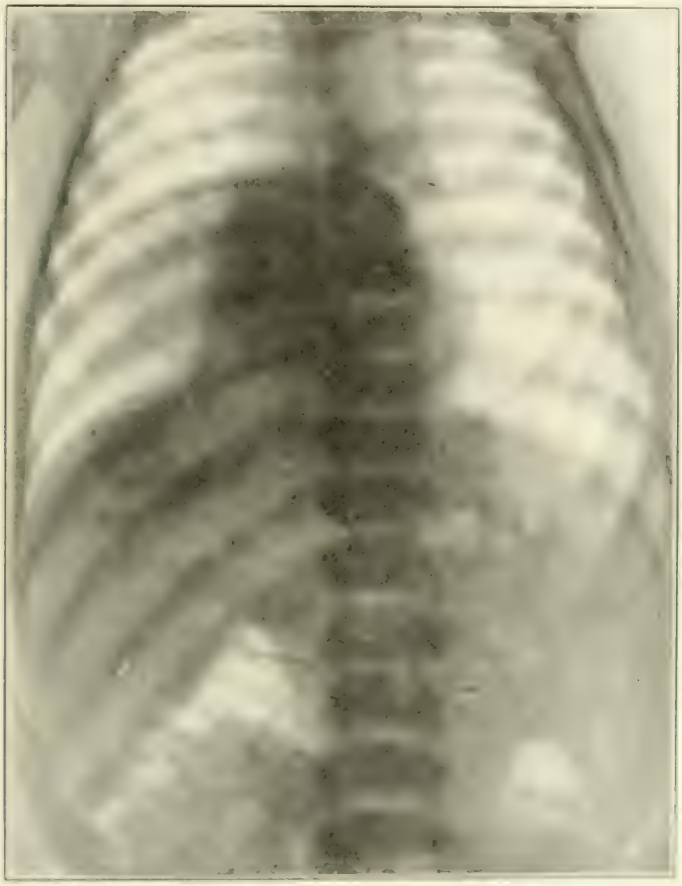


FIG. 1. Antero-posterior roentgenogram in the case described as Hilton and Fenwick. (See Fig. 2.)

where there are large hernias on the left side there is usually evidence of considerable displacement of the heart to the right (Fig. 2). The physical signs over the lungs vary considerably. Sometimes those of a pneumothorax seem to be present. At other times, fluid is suggested as in the case of Hilton and Kinnicutt which was actually aspirated and yellow fluid obtained.

When the stomach is herniated into the right side of the chest

as in the collected series of this paper, we may hope to find a layer of gastric tympani between the lung resonance and the area of liver dullness. Dietlin found these signs in his adult patient but in the infant reported in this paper, several examinations have failed to elicit these signs. The absence of gastric tympani from its normal site may be a helpful sign but this absence may be obscured by the presence of gas in a distended splenic flexure.

The fluoroscope, or x-ray plates taken after the administration of barium will of course clear up the diagnosis in most if not all

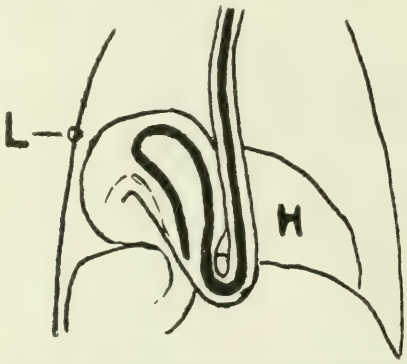


FIG. 9. Showing the heart (H) displaced far to the right. L. denotes the left nipple. This sketch affords an interesting comparison with Fig. 5. (From Hirsch; see Biblio. ref. 10.)

of these cases. Even without barium the diagnosis can often be made with the x-ray. The line of the diaphragm may show a portion regular and a portion blurred with a gas shadow above. The hernial sac as a whole may be distinguishable as well as the fluid or gas contained therein. Dietlin and Knierim called attention to a curved line rising from the liver shadow about in the right nipple line and curving up and over into the shadow of the sternum. (Fig. 2.) In questionable cases, insufficiency or eventration of the diaphragm must be borne in mind with its markedly upward and yet symmetrical displacement of an entire half of the diaphragmatic arch together with the organs situated below that half. Here of course there is no loss of contour of the diaphragm nor do gas shadows appear above the liver shadow. A point usually strongly in favor of the diagnosis of hernia is made when lung tissue is seen through the shadow of the gas-filled stomach. Also evidences of gastrointestinal obstruction found often in hernias are not found in cases of insufficiency.

PROGNOSIS. However, diaphragmatic defects may exist for years without harm to the subject. Latta[9] found that ten of the

127 cases he collected lived to adult life and one lived to the age of 70. In most of these adult patients, the diaphragmatic defect was unrelated to the cause of death, the subjects apparently suffering no inconvenience from the lack of a perfect diaphragm. Either the misplacement of the organs was not enough seriously to disturb the pulmonary and cardiac function, or the unaffected lung had been so able to function as to compensate for the loss of function of the other lung. It is also quite probable that many people with a small defect of the right side of the diaphragm go through life symptomless due to the fact that the liver may protect the opening and thereby prevent the herniation of a hollow viscus. But even where the diaphragmatic defect is such as to permit herniation enough to cause distressing symptoms, the condition is not necessarily incompatible with life nor irremediable, although noted authors still write that "the condition is not amenable to treatment."

TREATMENT. Many reports of operative cure of left-sided diaphragmatic hernias are now to be found in recent literature. In the majority of cases, it has been possible to restore the organ or organs to the abdominal cavity and close the opening in the diaphragm. Keith[3] cured his patient (No. IV in our series) of a right-sided true hernia involving the stomach by operating through the chest from behind and tying off the hernial sac after first reducing the hernia in a preliminary operation via the abdominal route. DeCourcy[4] approached a somewhat similar hernia (No. III in our series) from below the diaphragm in front, pulling down the herniating stomach and putting a purse-string suture around the diaphragmatic defect. Downes[11] found a seven year old boy whose entire stomach had passed through the esophageal opening in the diaphragm and rested on the left half of the diaphragm. Being unable readily to replace the stomach in the abdomen, he did a gastroenterostomy through the hernia opening and relieved the symptoms of vomiting which had lasted for over five years.

However, operations of this sort are very serious affairs, and the patient must be a pretty good surgical risk before a curative operation can be undertaken. Accordingly it is often necessary first to attempt to build up the patient by proper feeding methods and proper hygiene.

In this expectant treatment of cases of diaphragmatic hernia, particularly of the right side, there are several facts that must be borne in mind.

1. Crying tends to increase intrathoracic tension and accordingly may increase the extent of the hernia.

2. The stomach is in an abnormal place and position and probably cannot hold as much at a time as when in the normal position. And particularly in right posterior hernias, there is apt to be a sharp angulation at the lower end of the esophagus which may cause definite obstruction with symptoms closely resembling those of cardiospasm. Hence, feeding with small quantities given very slowly and at frequent intervals seems to be indicated.

3. Where the hernia is large, keeping the patient in an erect or semi-erect position may greatly relieve the respiratory embarrassment which is marked when the patient is prone.

4. Should a severe respiratory crisis of extreme embarrassment to breathing occur, it may likely be due to an accumulation of gas in a herniating hollow viscus, a condition possibly relievable by the passing of a rubber tube.

And finally, it might be advisable in certain cases, immediately before doing a corrective operation on a case of diaphragmatic hernia, to do one or more artificial pneumothoraces on the affected side, primarily to adjust the heart to the shock that is incident to a chest operation, but also possibly to reduce somewhat the size of the hernia.

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10. Hirsch: Zur Klinischen Diagnose der Zwerchfelhernia, München. med. Wchnschr., p. 996, 1900. Quoted by Eppinger, No. 1 above, p. 142.

11. Downes, W. A.: Congenital Hernia of the Diaphragm, Surg., Gynec. & Obst., 27, p. 393, Oct., 1918.

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HEMOLYSIS FOLLOWING TRANSFUSION*

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The development in human blood serum of antibodies capable of agglutinating and hemolysing the red blood cells of other individuals, has been shown to take place very early in life. These antibodies, known as isoagglutinins and isohemolysins, develop in infant serum quite independently of the mother's serum. The two kinds of reactions are dependent on each other to the extent that hemolysis does not develop unless corresponding agglutination occurs and the susceptibility to lysis only appears in cells which are already susceptible to the corresponding agglutination. This has been shown to be true by Moss.[1]

It has been noted that isoagglutinins occur with greater frequency in infancy than do the corresponding isohemolysins and that as the child grows older they make their appearance in a far greater number of cases, until the period of two years is reached, at which time practically all human beings have their full quota of agglutinins and hemolysins.[2] All persons can then be definitely divided according to their agglutination reactions into one of four biologically distinct groups, which are hereditary in character and follow the Mendelian principles of transmission.[4] Once the group is established, it remains so throughout life and is not affected by disease.[5]

Landsteiner[6] in 1900 divided all human beings into three groups by agglutinating property of their red blood cells. In 1902 Decastello and Sturli[7] examined a large number of persons over six months of age and

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1. Moss, W. L.: Studies in Isoagglutination and Isohemolysis, p. 21. Myers, Baltimore.
2. Hektoen, L., and Q. ...: Experiments in Isoagglutination and Isohemolysis, Jour. Infect. Dis., 11:1-23, 1912. Moss, loc. cit.
3. Landsteiner: Centralbl. f. Bakt., 27:357, 1900; quoted by Moss and Ottenberg.
4. Von Dungern and Hirschfeld: Physik. Ztschr., 6:284, 1910. Hirschfeld, H.: Hereditary Blood Qualities, Jour. Immunol., 6:1, 1921.
5. Hektoen, Jour. Exp. Med., 6:61, 1901.
6. Landsteiner, K.: Über Agglutinationserscheinungen normalen menschlichen Blutes, Wien. klin. Wchnschr., 14:1132, 1901.
7. Decastello, A., and Sturli, A.: Über die Isoagglutinine im Serum gesunder und kranker Menschen, Münch. med. Wchnschr., 49:1090, 1902.

corroborated the work of Landsteiner, but noted in addition several cases which did not fit into any one of the three groups. In 1907 Jansky showed that these cases belonged to an entirely different group, which he called Group IV and thus established the present accepted nomenclature of blood groups. Since that time it has been repeatedly emphasized, that to avoid dangers connected with transfusion, other than those which cannot yet be avoided by any technic, such as chills and fever, both the donor and recipient must belong to the same group, that is, the serum of the donor and recipient must not contain isoagglutinins or isohemolysins capable of acting on each others cells to produce agglutination or hemolysis.

The occurrence of isohemolysis without isoagglutination has not been observed in man. Experimentally, however, Ottenberg and Thalheimer [8] have produced isohemolysis in cats whose serum did not agglutinate. This was done by transfusing blood from one cat to another, whose blood before the transfusion was entirely compatible with that of the first. This has not yet been shown to be true for man. The production of isohemolysins and the iso-agglutinins in human blood by means of transfusion is demonstrated by the following case reports:

Case 1.—J. H., a girl, aged 18 months, a first child, born of healthy parents, was admitted to the hospital with signs and symptoms indicating a nasopharyngitis and bilateral acute otitis media. Both ear drums were incised, and much pus was evacuated. One week after admission there were signs of involvement of the mastoid process, and it was decided to perform a blood transfusion because of the poor general condition, and to operate on the mastoid process. The child's and the mother's blood were reported compatible, and the child was transfused immediately after the operation, Dec. 24, 1921. About 180 c.c. of citrated blood obtained from the mother was introduced, with no reaction, either immediate or delayed. Twenty days after the first transfusion, Jan. 13, 1922, transfusion was again performed, the mother again acting as donor. No tests were made, since the first transfusion had resulted in no symptoms, and it was thought perfectly safe to use the previous donor. After the child had received 130 c.c. of citrated blood, she began to vomit, became cyanotic and unconscious, the breathing became labored, and the clinical picture was that of shock. The transfusion was stopped, stimulation was resorted to, and at

8. Ottenberg, R., and Thalheimer, W.: Studies in Experimental Transfusion, J. M. Res. **33**: 213 (Nov.) 1915.

the end of two hours the child became conscious; but the cyanosis persisted. Six hours after the transfusion, the bladder was catheterized, and about 30 c.c. of urine containing hemoglobin was obtained. Microscopic examination did not reveal any erythrocytes, though blood shadows could be made out. Bleeding also took place from the incision into the mastoid process and from the lips. The condition was critical. No urine was passed until the next morning; but when the bladder was again catheterized, about 10 c.c. of smoky looking urine was obtained. Jaundice developed the following morning, which persisted for several days. The temperature rose to 106 F., and gradually returned to normal in four days. The vomiting and hemoglobinuria, as well as the other symptoms, gradually disappeared, and the child made a complete recovery. The blood of the child and that of the mother were retested and found to be incompatible. The mother belonged to Group II, and the child to Group I.

Case 2.—In January, 1917, a man, aged 22, suffering from hemophilia, underwent transfusion with 50 c.c. of blood, by the syringe method, from a friend, reliance being placed solely on mutual agglutination tests. There was no reaction, and the patient's urine was examined and found normal after the transfusion. Approximately one month later, another transfusion of the same amount was given from the same donor, no further tests being made. Transfusion was followed by collapse, cyanosis, urticaria and hemoglobinuria. Samples of blood obtained from the patient and the donor about one week after the second transfusion showed that the patient's serum strongly agglutinated the red blood cells of the donor. The first transfusion apparently stimulated the production of isoagglutinins and isohemolysins, which produced their effects at the time of the second transfusion.

Comment

Attention is here called to the occurrence of two cases in which severe reactions took place in patients who were recipients of blood from donors who had previously acted as such without any reaction having taken place following the first transfusion. The mechanism of the reaction following the second transfusion may best be understood by examining Table I, in which are set forth the characteristics of the various blood groups. In his work on blood groups, Landsteiner* brought forth the hypothesis that there were present, in all human blood serums, two sets of isoagglutinins and isohemolysins, and in all red blood cells two sets of cell receptors. It will be seen that Group I has both agglutinins and hemolysins in its

serum, while its cells contain neither one of the receptors A and B; Group II has agglutinogen A and iso-agglutinin and isohemolysin b; Group III, agglutinogen B and iso-agglutinin a, while Group IV, the rarest group, contains both agglutinogens A and B, and no iso-agglutinin or isohemolysin.

It has been shown repeatedly that the red blood cells attain their group characteristics, known as receptors, or agglutinogens, very early in life. Since the mother and child belonged to different groups, why is it that no reaction took place following the first transfusion reported above? The answer lies in the fact that the child's red blood cells, because they belonged to Group I, had neither one of the susceptible substances and, therefore, its own cells could not be

TABLE 1.—JANSKY CLASSIFICATION

Group	Agglutinogens Hemolysinogens	Iso-agglutinins Isohemolysins
I	None	a and b
II	A	b
III	B	a
IV	A and B	None

agglutinated or hemolyzed. Its serum, on the other hand, had not yet developed the antibodies belonging to its group (a and b), or they may have been present, but in such weak titer that no significant reaction took place. The group to which the child belongs (Group I) was incompletely established at the time of the first transfusion, while twenty days later the child's serum had acquired its full quota of antibodies, presumably as a result of the stimulation of the first transfusion. The development of these iso-antibodies apparently can take place in a shorter period of time, as is proved by one of Lindeman's [10] cases, in which hemolysins developed after a period of five days. It must be stated that the first grouping reported from the laboratory was incorrect. Both the mother and the child were then reported as belonging to Group I. Subsequent determinations showed that the mother belonged to Group II, and the child to Group I. It is to be regretted that the second transfusion was performed without a retest of the donor and recipient. These cases and others of a similar nature in the literature demon-

10. Lindeman, Edward: Blood Transfusion, J. A. M. A. **62**: 993 (March 28) 1914.

strate conclusively the danger confronting us, chiefly in the case of children, whose blood groups are incompletely developed, when tests for compatibility are not repeated before each transfusion.

It was important to determine the exact antibody content of the mother's and child's blood. Accordingly, blood was obtained from the veins, separated into serum and cells, the cells were twice washed with isotonic saline solution, and a 5 per cent. suspension of each one's cells was made.

Tests were performed, using the suspensions given in Table 2.

TABLE 2.—TESTS PERFORMED

0.1 c.c.	5%	suspension	of	child's	cells plus 0.2 c.c.	mother's	serum
0.1 c.c.	5%	suspension	of	mother's	cells plus 0.2 c.c.	child's	serum
0.1 c.c.	5%	suspension	of	mother's	cells plus 0.2 c.c.	Group II	serum
0.1 c.c.	5%	suspension	of	child's	cells plus 0.2 c.c.	Group I	serum
0.1 c.c.	5%	suspension	of	child's	cells plus 0.2 c.c.	saline	
0.1 c.c.	5%	suspension	of	mother's	cells plus 0.2 c.c.	saline	

All were incubated for one hour at 37.5 C. No reaction took place in any tube except that containing mother's cells and child's serum, this tube showing both agglutination and hemolysis. This discloses that after the second transfusion the child's serum was lytic for the mother's cells, and explains the intravascular hemolysis.

The hypothesis advanced by Landsteiner of the presence in human blood serum of two sets of agglutinins and hemolysins, and in the red blood cells of two sets of cell receptors was, confirmed by Decastello and Sturli[1] in 1902 and later investigators. Koeckert,[2] in 1920, in carefully controlled experiments, proved by absorption methods the existence of these two agglutinins and hemolysins, known as a and b, and the two agglutinable substances in the red blood cells (otherwise known as cell receptors or agglutinogens), A and B. By this method of differential absorption one may remove from any serum either one or both of its two agglutinins, and with the agglutinins the corresponding hemolysins. This may be done by combining the serum of one group with the red blood cells having receptors for the agglutinins contained in that serum.

Since the child belonged to Group I, its serum could have contained both agglutinins and hemolysins a and b

[illegible]

To determine which of these were present, known Group II and Group III cells (containing agglutinogen A and B, respectively) were taken, and to 0.1 c.c. of a 5 per cent. suspension of these cells, 0.2 c.c. of child's serum was added and incubated as explained above. Apparently both a and b agglutinins and a and b hemolysins were present, since agglutination and hemolysis of Group II and Group III cells occurred to about the same degree. This shows that at the time of the second transfusion, the serum of the child contained a and b agglutinins and hemolysins, and its group was now fully established.

Pepper and Nisbet,[12] in 1907, reported a case of fatal hemolysis following direct transfusion of blood by arteriovenous anastomosis, blood groups being undetermined. This was a second transfusion, the first one having been followed by very slight reaction as judged by the amount of hemoglobin in the urine.

Lindeman,[10] in 1914, reported a case in which the first transfusion was not accompanied by any reaction, and tests showed no hemolysis, while the second transfusion, five days later, using the same donor, bloods not being retested, was followed by hemoglobinuria. Tests now showed hemolysis of the donor's cells by the recipient's serum. This shows the development of iso-antibodies in five days following the first transfusion. Recovery followed.

Thalheimer,[13] in 1921, reported a case of hemoglobinuria after a second transfusion with the same donor in a child, aged 6 years. Recovery followed. In this case a direct test, prior to the first transfusion, disclosed no agglutination. Eighteen days later another transfusion was done, and severe hemoglobinuria followed. The father belonged to Group III, and the child to Group I. Here the success of the first transfusion either was due to the presence of weak agglutinins in the child's serum, or they had not yet developed.

The conditions which require a second or repeated transfusion are not rare and, therefore, the foregoing observations are important. Close analysis demonstrates that all the reactions were due to the transfusion

12. Pepper, William, and Nisbet, Verner: A Case of Fatal Hemolysis Following Direct Transfusion of Blood by Arteriovenous Anastomosis, J. A. M. A. **49**: 385 (Aug. 3) 1907.

13. Thalheimer, William: Hemoglobinuria After a Second Transfusion with the Same Donor, J. A. M. A. **76**: 1345 (May 14) 1921.

of blood cells which were susceptible to agglutination and hemolysis by the patient's serum. There is current opinion that the criterion of compatibility of bloods lies in testing the donor's cells against the recipient's serum; and more thoroughly to safeguard against any accident, it is also advisable to test the recipient's cells against the donor's serum. While these mutual tests are satisfactory for a first transfusion, the results of the tests made before the first transfusion cannot be relied on for the second transfusion. The tests must be done over again, since new antibodies may have developed after the first transfusion.

According to Karsner's [14] observations, mutual tests are not as safe as group tests. In cases of chronic anemia, it was shown by Karsner that the agglutinin titer of the patient's serum may be so low as not to produce agglutination on the slide, though the red blood cells of these patients contain their full cell receptors, and transfusion in such cases results in intravascular agglutination and hemolysis. This has not been reported by others, who have found intravascular effects only when the serum of the patient contained the demonstrable antibodies.

In the case of infants and children, it is not at all uncommon to find weak agglutinating serums; and sometimes adults, especially those belonging to Group III [15] have a similar lack of agglutinins in their serum, and mutual tests may be negative, yet intravascular hemolysis will take place. Testing the group to which a child belongs by testing its corpuscles against known strong serums, particularly in the case of children under 2 years of age whose groups may be incompletely established as regards agglutinins, does away with the danger of mistakes due to weak agglutinins in a child's serum. However in the case of children (and only in the case of children), if, instead of mutual tests, the method of grouping donor and patient by reference to known agglutinating serums of Groups II and III has been followed, it is necessary to repeat these grouping tests, for the agglutinogens of the blood cells of young children are not always fully developed. The foregoing cases illustrate the rapid development of a previously absent group character—agglutinins

and hemolysins—(not a change of group). There are no observations reported as yet to indicate whether agglutinogens can be developed as rapidly.

Numerous authors have established that the agglutinogens or group specific substances residing in the cells appear earlier and more completely than the group specific substances present in the serum. In the mutual tests the serum qualities are chiefly depended on, and these, as has been pointed out, are often incompletely established in the case of infants. Reliance, therefore, is placed on a method which has inherent defects. In determining the group to which a child belongs, one always should select strong serums of the known Groups II and III, and reliance is then placed on the qualities of the red blood cells which develop earlier and more completely. The mutual or direct tests may, however, be used as a check on the determination of the blood groups, but by itself is not as reliable as the grouping method. Moreover, the grouping method is by far the simpler and the less time consuming.

CONCLUSIONS

1. Iso-agglutinins and isohemolysins originally absent or weak may develop to full strength after a single transfusion.

2. Because the serums of infants and children often possess only weak iso-agglutinins and isohemolysins, or contain none, it is important to determine the group to which the child and the donor belong, by testing their red blood cells against known strong Group II and Group III serums.

3. The mutual tests may be used as a check, but should not be solely relied on, particularly in the case of infants and children, and especially for second or third transfusions in the same individual.

4. The tests should be repeated before each transfusion in the case of children.

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CONGENITAL DUODENAL OBSTRUCTION AND MALROTATION OF THE INTESTINE

REPORT OF CASE*

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In this report the clinical rather than the developmental aspects of congenital duodenal obstruction will be emphasized. It seems that enough cases have been recorded to warrant giving a more definite clinical picture, and this may serve to center interest in them as clinical cases rather than as pathologic specimens. Unfortunately, the first few days of life are a veritable shadowland for diagnosis and treatment. The infant that seems barely holding on to life may be a thriving youngster a few days later, and, on the other hand, sudden and unexplained exitus of a baby apparently not very ill is an all too frequent occurrence. Similarly, at this time of life exploratory laparotomy is an adventure. It is, therefore, with some hesitancy that the effort is made to group the striking clinical features of congenital duodenal obstruction and to suggest that at least some of the cases may be brought within the reach of surgical assistance. Perusal of the literature, in addition to the study of a single case, forms the background for the discussion and conclusions.

From the clinical standpoint, the possible duration of life of infants suffering from duodenal obstruction is of first importance. As far as this is related to the anatomic anomaly, the duration of life is dependent on whether there is stenosis (complete occlusion of the intestinal tract) or merely stenosis (partial obstruction). Of thirteen cases of stenosis collected by Kreuter in 1905, four patients lived for a week or more.[1] A search of the literature since 1905, probably not complete, of cases of partial obstruction which the patient live more than a week, has revealed an even greater number.[2] Four infants died during the second week of life, and three during the second month; four others lived from one to nine months, one for twelve months

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1. Two infants lived seven days, one lived twelve days and one six months.

2. The writer will be grateful for the privilege of including in this report any cases of obstruction due to congenital malformation of the duodenum which have not been recorded in the literature.

one for eighteen months and one for two years.[3] The mere duration of life is emphasized because it indicates that in some cases there is at least time for surgical intervention.

Efforts at treatment have been made. Colwell, in 1912 recorded five cases in which enterostomy had been done, although unsuccessfully. Commenting on the reports of Keith and Buchanan of infants living nine and eighteen months, he remarked, "it would seem that cases should be subjected to laparotomy, and, if possible, gastro-enterostomy should be performed." Indeed, since then such an operation has been done successfully. Ernst, in 1916,[4] operated on an infant 11 days old. There was an obstruction "at the upper side of the transverse mesocolon" and Ernst performed a duodeno-entero anterior anastomosis. Eleven months later the child was a "vigorous well developed youngster."

The symptomatology of cases living more than a week depends on the location and degree of obstruction. When the obstruction is situated below the ampulla of Vater, the vomitus is bile stained. This is emphasized by nearly all the authors who considered the symptomatology of the cases they reported.[5] Bradford believes that "vomiting occurs after the lapse of a longer period following feedings than does the vomiting caused by stenosis higher in the tract." In nearly all cases there was difficulty in excluding pyloric stenosis, and in many cases that was the diagnosis made. Tumor was mentioned by only a few authors; it was a vague sign.[6] Peristaltic waves were more frequently found. Fecal stools, the occurrence of the residue of milk digestion or the continuance of meconium stools beyond the usual period were helpful in determining partial or complete obstruction. Prolongation of life, despite an almost complete obstruction was a surprising

3. Commandeur: Lyon méd. **114**:423, 1908. Freeman, R. G.: Arch. Pediat. **27**:37, 1910. Shaw. H. L., and Baldauf, L. K.: Tr. Am. Pediat. Assn., 1907, p. 36. Weber: München. med. Wchnschr. **60**:212, 1913. McClanahan, H. M.: Arch. Pediat. **25**:533, 1918. Stolte, K.: Monatschr. f. Kinderh. **12**:341, 1913. Colwell, E. M.: Quart. J. Med. **5**:401, 1911. Spriggs, N. I.: Guy's Hosp Rep. **66**:143, 1912. Van Der Bogert: Arch. Pediat. **33**:194, 1916. Schroder, C. H.: J. A. M. A. **78**:1039 (April 8) 1922. Cautley, E.: Brit. J. Child. Dis. **16**:184, 1919. Bradford, O. F.: J. Missouri M. A. **15**:307, 1918. The case of Helmholz and Little (Johns Hopkins Hosp. Bull. **16**:231, 1905) should be included, although it was a complete obstruction. A gastro-enterostomy was done and the child lived eight days.

4. Ernest, N. P.: Brit. M. J. **1**:644, 1916.

5. A possible exception to this statement is Van Der Bogert's case. In an infant, 4½ months old, with a duodenal obstruction 2½ inches from the pylorus "there was no appearance of bile in the vomitus, although unfortunately no chemical tests were made."

6. Loc. cit. Cautley and also Schroder.

reason. In Cautley's case, in which the child lived twelve months, "the second part of the duodenum was extremely stenosed, merely admitting the passage of a probe." And Spriggs, performing a necropsy on an infant 9 months old, found a diaphragm occluding the lumen of the duodenum; and, as he remarked, although there was "no evidence of an orifice in this diaphragm, the history of the case proves that some opening must have existed." The uncertainties of abdominal diagnosis, in general, at this early age, combined with variations depending on the position and degree of obstruction, make it very difficult to outline a clear cut clinical picture. One might be tempted to offer a crude rule of thumb, that a symptom complex suggesting but not typical of pyloric stenosis or pylorospasm, in a desperately sick infant, should raise the question of an obstruction in the upper part of the small intestine.

The etiology of duodenal obstruction has been fully [illegible].[3] Many of the anomalies and the theories to explain them are referable to conditions within the lumen of the intestine, valves, folds of mucous membrane, failure of absorption of embryonic epithelial plugs, etc. The case to be reported was not studied from that angle, and although it is extremely unlikely, such a factor might have been operative in addition to malrotation.

REPORT OF CASE

History.—Baby K. was born on the obstetric service of the New York Nursery and Child's Hospital, Dec. 21, 1926. Forceps of pregnancy were used, delivery by cesarean section during the eighth month of pregnancy. The resistance baby weighed five pounds and appeared well developed. When 7 days old the child was transferred to the pediatric service with the history of [illegible] pounds loss of weight and vomiting of all food since birth. The infant was very [illegible] in color and not [illegible].

Course.—Dr. Anderson, the resident physician, noted that the baby was emaciated, the tongue dry, the fontanel sunken and the liver and spleen palpable. The infant lived twenty-two days after admission to the pediatric service. Although occasional days passed without vomiting, persistent bilious vomiting was the striking condition. Despite numerous examinations [illegible] gastric contents. Except on numerous occasions also revealed [illegible] undigested food, it [illegible] as much as from 3 to 4 ounces of "thick red wine material." At first the stools were yellow and indicated the passage of food through the intestines; toward the end they became watery and green. The temperature elevation was not constant. It showed no periodicity [illegible] at times normal and a [illegible] Andrew suffering the results of the [illegible]. Three days before death [illegible] severe acute [illegible] The exact cause could be left. Stools were [illegible] for a few days. It is hardly necessary to detail the operative measures employed [illegible] unfortunately not [illegible] the peritoneal cavity and [illegible] to be useful in [illegible].

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3. Ravenel, E.: Die Angeborenen Verengerungen u. Verschliessungen des Duodenums, Ztschr. f. Chir., Leipz., 1902, lxvi, 1. Ladd, W. E.: Congenital Occlusion of the Duodenum, Boston M. & S. J., 1905, clii, 1. Child, C. G., III: Congenital Obstruction of the Duodenum, Ann. Surg., 1913, lvii, 1. Bland-Sutton, J.: Congenital Obstruction of the Duodenum, Lancet, London, 1913, ii, 1. Fisher, A. A.: Congenital Obstruction of the Duodenum, Surg., Gynec. & Obst., 1913, xvii, 1. Spriggs, E. I.: Congenital Occlusion of the Duodenum, Arch. Pediat., 1913, xxx, 1. Cautley, E. W.: Congenital Occlusion of the Duodenum, Lancet, London, 1913, ii, 1. Cautley, E. W.: Congenital Occlusion of the Duodenum, Lancet, London, 1913, ii, 1. [illegible]

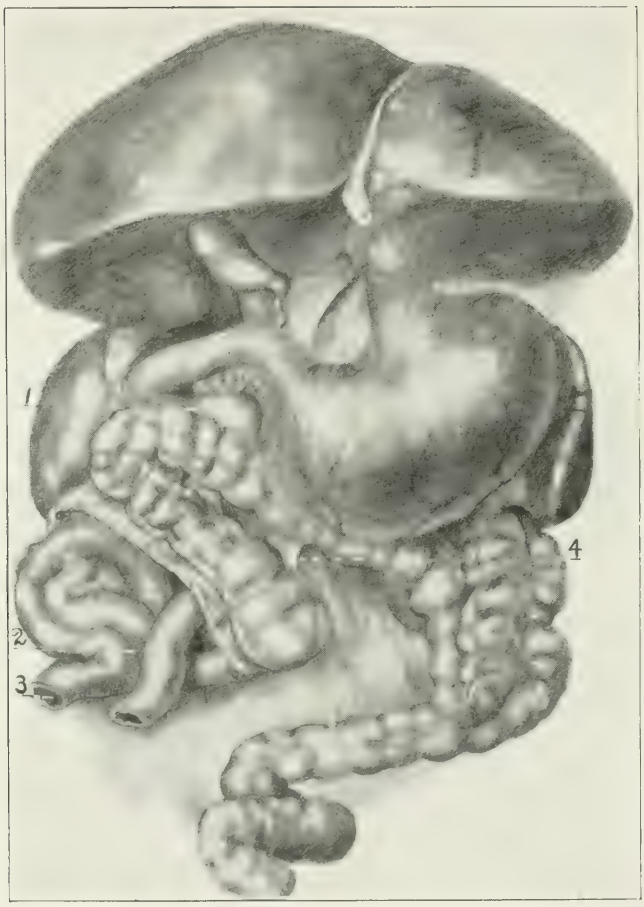

Fig. 1.—The liver has been pulled upward and the transverse colon downward. This gives the impression that pressure occurred lower down in the duodenojejunum than was actually the case. (1) Sharp duodenojejunal angle; (2) jejunam; (3) lower part of ileum; (4) band attaching cecum to posterior abdominal wall.

Diagnosis.—The diagnosis lay between pyloric stenosis and obstruction below the ampulla of Vater. Bilious vomiting, pointing to obstruction at the pylorus sphincter, was the striking symptom and most of those who examined the infant favored the diagnosis of obstruction. A second transfusion preliminary to exploratory laparotomy was planned when the infant died.

Autopsy.—Aside from the intestinal tract the autopsy is not of interest. The small intestine occupied the entire right half of the abdomen. The cecum was situated to the left of the midline beneath the transverse colon (Fig. 1). Drawing the cecum downward and to the right, brought out a firm, rather tough band, attaching the cecum to the posterior abdominal wall. The ileum entered the cecum from right to left. The stomach was much dilated and the pylorus was wide and flabby. The dilatation of the first portion of the duodenum was even more pronounced than is indicated in the sketch.* The third portion of the duodenum, instead of curving gradually upward, turned to the left, forming a sharp, mushroom-shaped angle. To explain these relations

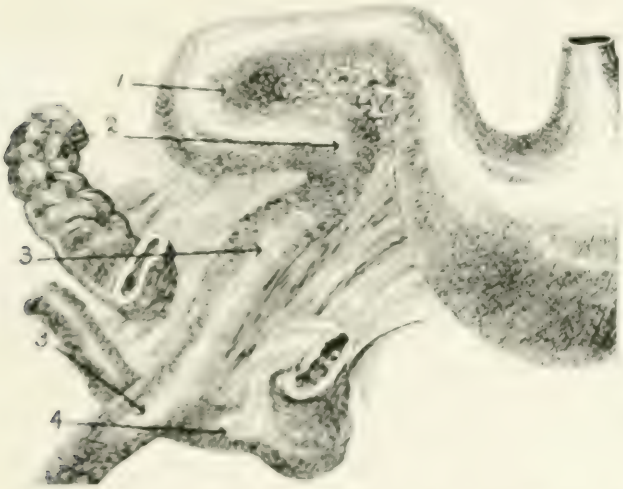

Fig. 2.—Stretching colon away and pulled back to show arrangement of obstruction. (1) Dilated duodenum; (2) duodenojejunal angle; (3) ligament; (4) ileum.

*Records the third part of the duodenum was crossing over the vertebral column and formed by the transverse or second part of the duodenum and the continuous loop of the intestine. As this loop of intestine continued downward, it emerged, clamped between the last few inches of the ileum terminally and the cecum and ascending colon externally. One may picture the ileum and the ascending colon as the blades of a scissors (Fig. 2). The junction of ileum with cecum to correct for the error, the junction of ileum with the ascending colon was downward instead of upward. Figure 1 shows the ascending colon cut and pulled back uncovering the duodenum as it crosses the spine. Thus, there were combined as the mechanism of the obstruction: (1) the acute duodenojejunal angle; (2) the crossing of the vertebral column; and (3) the ligament

†The small size was due to the preserved and somewhat shrunken specimen.

(3) the binding down of the cecum to the posterior abdominal wall. The fixation of the cecum prevented free mobility, and a freely movable cecum might have exerted less pressure on the small intestine.

It is simpler to describe the anatomic conditions determining the obstruction than to trace their pathogenesis. The explanation of the mechanism of obstruction rests on the determination of the primary factor in the malrotation of the cecum and ascending colon. It will be recalled that in early fetal life the alimentary canal is a vertical tube. As development proceeds, the colon, which is at first on the left side, rotates about the mesenteric axis and the cecum passes across the duodenum and finally descends to the right iliac fossa. "This rotation may be arrested temporarily or permanently in any position during its circuit." [9] In the case presented there are two possibilities. First, there might have been a localized peritonitis that produced a fibrous band maintaining the cecum in the position characteristic of an earlier period of fetal life, that is, to the left of the median line (Fig. 1). According to this explanation, the fibrous band, or rather the inflammation responsible for it, would be considered the primary factor preventing normal rotation of the large intestine. Or, secondly, there might have been some other unknown primary factor interfering with normal rotation; according to this assumption, the fibrous band would be considered the result of a secondary contraction of a loose peritoneal fold. The sharp duodenojejunal angle was surely secondary; most probably it was due to the drag exerted by the small intestine. The loops of intestine hung from the mesentery as from a pedicle instead of spreading out fan shaped in the normal fashion. In either case failure of the intestine to rotate completely was the immediate cause of obstruction since it left the cecum in such a position that pressure upon the duodenum was unavoidable.

DISCUSSION AND CONCLUSIONS

Duodenal obstruction in infants, and especially in new-born babies, embraces too many variant factors to warrant generalizations. The most that can be expected, as far as diagnosis is concerned, is the determination of the presence of obstruction, whether it is partial or complete, and its approximate location. Recording the symptomatology may develop a clearer clinical picture. The results of surgical intervention depend chiefly on the complexity of the lesions. Surgeons who have seen the specimen doubt very much whether anything could have been done in the case described. In general, gastro-enterostomy is

9. Mayo, C. H.: Med. Rec. **81**:401, 1912.

the operation indicated. The duration of life in some infants with duodenal obstruction and the successful performance of gastro-enterostomy by Trust suggest that under favorable circumstances some cases may be amenable to surgical treatment. The cause of the obstruction in the case reported was malrotation of the intestine; whether the malrotation was primary or due to a fibrous band binding the cecum to the left abdominal wall, is controversial.

PULMONIC AND CARDIAC CHANGES FOLLOWING INOCULATION WITH FOREIGN PROTEIN

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I. ADULTS

THOSE of us who were doing intensive investigation of early pulmonary changes in the type of infection prevalent during the great pandemic, were struck by the prevalence of a high percentage of these cases showing parenchymal changes without symptoms and the almost universal involvement of the hilums in all cases, even when there were no subsequent pulmonary sequelae. Further study of these cases showed that mottling of mediastinal and bronchial root tissues still remained several months after the subsidence of all clinical signs. Lord, in his chapter on circulatory disturbances, states that "inflammatory hyperemia, too slight in degree to be termed pneumonia, may be seen in the course of influenza and typhoid fever." Localized and sometimes general pulmonary congestion occurs, as is well known, after injection of tuberculin. Pulmonary mottling is quite commonly seen after inhalation of certain substances, as in hay fever. This is not so much by reason of their mechanical trauma as by their anaphylactic import. In the routine *x*-ray examination of influenza cases, attention was drawn to a radiogram in which general mottling was of a different type from the usual case. Two changes were sufficiently great to warrant further investigation, with the following interesting history:

The patient had received the usual dose of 0.5 c.c. of triple typhoid vaccine (army), and within thirty-six hours he was prostrated, and developed headache, malaise, back pains, short irritable cough and temperature (not a rare experience). On physical examination there was increased dulness and bronchovesicular breathing, and a few indeterminate rales were found from the 4th to the 2nd interspace on the left side. Clinically, because of the epidemic, a diagnosis was made of influenza with possibly a bronchopneumonic process. The clinical findings and the history of inoculation made an absolute diagnosis seem undesirable. As was the rule at this time during the epidemic, the patient was immediately examined radiologically. The plates showed a localized area of increased density from the 4th to the 2nd rib on the left side, and as there were none of the characteristic diaphragmatic and cardiac reactions to which Honeij has called attention, we felt that a definite diagnosis of influenza was unjustifiable.

Within thirty-six hours the temperature dropped to normal and the chest cleared up completely. Subsequent radiograms showed that the process was much improved and mottling was almost absent. Following this finding, the next 8 cases inoculated with typhoid vaccine were examined radiologically before inoculation and forty-eight hours later. Seven of these cases were supposedly "normal" chests; the eighth was one of extensive and non-active tuberculosis. The following findings were obtained:

Not one of them failed to reveal increased density, either pulmonary or hilum. In 6, this was general in character; in 6, the apices were involved; in 2, the middle thirds of both lungs were affected; in 1, the bases were involved. In 6, the upper aspect of the hilum was distinctly enlarged and mottled. In 7, the middle portion of the hilum showed these changes, and in 7 the lower portion of the hilum. In 5, the heart showed slight pulmonic dilatation; in 4, it showed right-sided dilatation. In 6, there was distinct increase in the peribronchial markings. In 1 case there was an increase in the size and density of the mediastinum; and in 1, glandular enlargement of the left middle hilum.

These incidental findings are analogous to those observed by investigators in cases of laboratory animals whose death was due to anaphylactic phenomena.

Infants and Young Children. Influenza Group

No.	Increased Density	Parenchymal Site	Heart Enlargement	Hilum	Remarks
1	General +	Left perihilum	+	Right hilum +	
	−	Perihilum + + +	−	+	
2	General +	Middle-right	+	Both hilums +	
	−	Left perihilum	−	−	
3	General +	Left perihilum	+	Left and right ?	Peribronchial type of increased density
	−		−		
4	General +	Left perihilum + +	+	+	
	+	Right middle +	−	−	
5	General +	Right apex	+	Both	Increased density limited to hilums and left apex
	−		+		
6	o	o	+	o	Only slight mottling of hilus present
			−		
7	o	o	o	o	No change observed
8	Slight General		+	Right Left perihilums	Heart only showed changes

Diphtheria Toxin Antitoxin Group

No.	Increased Density	Lobes	Heart Enlargement	Hilum	Remarks
9	Peribronchial +	Right apex	o	Right	
	−				
10	General +	All lobes	+ + +	Left + +	Questionable cardiac lesion
				Right +	
11	General	Upper right	+	Both	Left-sided cardiac enlargement
12	Local	Left upper	(Slight) +	Right	
13	General	Right base	Left sided + +	Both	
14	?	Left lower	Right sided (?)	Right	
15	Local	Right lower	+ +		
		Right middle		Both	
16	Local	Perihilum	+	Both	Upper mediastinal enlargement
17	Local	o	+	Both (?) +	
			−		
18	Local	Right upper	+	Right	
			−		
19	Local	Right upper	+	Both	Changes of upper mediastinum
			−		
20	o	o	Slight enlargement	+	
				−	
21	Local	Right middle	+ +	Both	
		Left upper			
22	Local	Right upper	+	Left	
23	Local	Right lower	+	Right	
			−		
24	Local	Right upper	o	Right	

II. Infants and Children

Further investigation of these phenomena, employing the same roentgenological technique, was carried out upon a group of infants numbering 24, of whom 16 had been prophylactically vaccinated with diphtheria toxin antitoxin. In this series the findings were essentially the same as in our adult group when typhoid vaccine was used.

As shown by the accompanying table, mottling was local or general and practically universal. In one case only the heart showed some reaction by dilatation.

The remaining 8 children were examined after prophylactic treatment with influenza vaccine. Here, too, our findings confirmed

our conclusions drawn from the work with typhoid vaccine and diphtheria toxin antitoxin.

In cases of food idiosyncrasy, as demonstrated by positive skin and constitutional reactions, with or without pulmonary anaphylactic signs, we have been able to demonstrate this intrapulmonary change as a concomitant anaphylactic phenomenon.

SUMMARY

Here we have an investigation covering a group of 33 individuals varying in age, the larger percentage of whom, after injection of foreign protein presented definite pulmonary changes and, in a smaller percentage, cardiac changes.

Paul B. Hoeber, 67–69 East 59th Street, New York

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A ROENTGENOLOGICAL STUDY OF TUBERCULOSIS OF LUNGS AND INTRATHORACIC GLANDS IN INFANCY AND EARLY CHILDHOOD.

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The high incidence of unsuspected tuberculosis in respiratory infections is strikingly brought home to the pediatrician conversant with an active roentgen-ray service. The routine application of roentgen-ray laboratory facilities serves to cut down the percentage of avoidable error in final diagnosis and helps materially in prognosis.

It is difficult to apply our knowledge of tuberculous changes gained through experience with adult pathology. In the infant early changes are much more massive, reactions more intense, and a definite proliferation of the lymphatic structures to disease confuse exact interpretation of actual pathology. Acute serous changes predominate. Chronicity is the exception. The early stage may be of difficult differentiation and only the subsequent course enlightens us as to the true etiology. Our classification shall be a simple one as it strikes a roentgenological observer. Generally speaking, changes fall into two headings: (1) those involving the glands; (2) those attacking the parenchyma.

1. *Glandular Changes.* These fall into three subdivisions, namely:

(a) Paratracheal.
(b) Peribulus.
(c) Peribronchial.

Finer classifications can be made, but a fusion of these processes is so general that for working purposes more divisions are cumbersome.

2. *Parenchymal Changes.* These are subdivided into three headings:

(a) Lungs.
(b) Pleura.

Glandular Tuberculosis. Generally speaking, we have found that the paratracheal glands are involved earliest in life, the perihilus somewhat later and the peribronchial latest in childhood. Sometimes the process confines itself to one region, occasionally more than one. In this case one site may be heavily involved and the other or others slightly so. Eventually an entire chain is affected.

Early Changes. Such a plate shows in the upper mediastinal region an evenly outlined shadow, rounded or elongated, depending upon the degree of congestive reaction and the number of glands involved. Smooth contours and unilateral shadows of even density characterize this stage. If the process is perihilus or peribronchial, the changes apply to these respective regions.

Conflicting shadows in this region are neoplasms and congenital anomalies, which are very rare, and thymus, which in contradistinction is usually bilateral, and in good plates shows a fine leaf-like arborization.

Differentiation from non-tuberculous processes at this stage is difficult and only subsequent events can clear up the diagnosis.

The second stage of changes, and that of more characteristic pathology is that due to necrosis and fibrosis. Outlines are irregular and blotchy, and so-called mottling is present. Occasionally, one may notice a zone of parenchymal congestion, and when these various changes are simultaneously present, the diagnosis of tuberculosis is probable. The ultimate outcome of these changes has been twofold; in one type, a retraction of shadow takes place, with an increase in density and an accentuation in the mottling; in the other type, a definite progression to parenchymal involvement with a picture which falls under the heading of mixed parenchymal tuberculosis.

Parenchymal Tuberculosis.

1. Pleural.
2. Pulmonary.

Pleural Changes. These have been of two types; an intralobar effusion, secondary as a rule to hilus gland pathology. The process is sharply defined usually between the upper and middle lobes. It subsides, as a rule, leaving a definite transverse, linear scar. However, not all linear scars are tuberculous.

The second type of pleuritis is usually found as a complication of a diffuse, pulmonary involvement, the picture of which overshadows pleuritic changes. These changes are either serous or fibrous. Serous deposition is usually in small quantities. Fibrous depositions take place in the form of fine filament-like bands or in rare instances, a diffuse, thick, plastic mass, not unlike that seen in the adult pleuritis. All combinations of these two types usually are present. At no time have we seen a primary, uncomplicated tuberculous serous or fibrinous pleurisy.

Pulmonary Changes. There are three types: (1) Bronchitic; (2) bronchopneumonic or lobular; and (3) lobar.

4. The bronchitic type is but a stage of pulmonary changes observed early in a general miliary infection, when the tubercle-

FIG. 4.—An example of annular shadow in an infant with a concomitant massive pneumonic process. Acute phase of bronchial infection.

FIG. 5.—Diffuse tuberculous infiltration of both lungs in a child

growth is barely discernible by plate methods and when death intervenes before full growth of tubercle has taken place. At this time, nearness are accentuated and somewhat congested in appear-

ance. This type of change is also seen with general miliary abscesses, due to a terminal sepsis. Should the disease be pro-

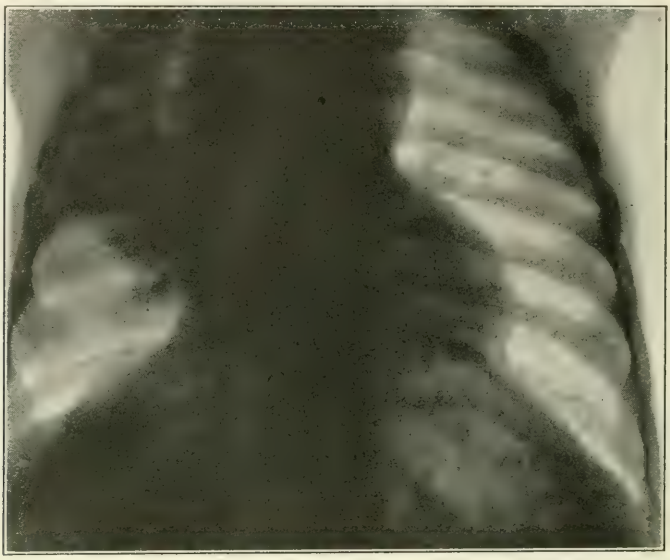

FIG. 3.—An example of paratracheal glands and a right sided perihilus pneumonia.

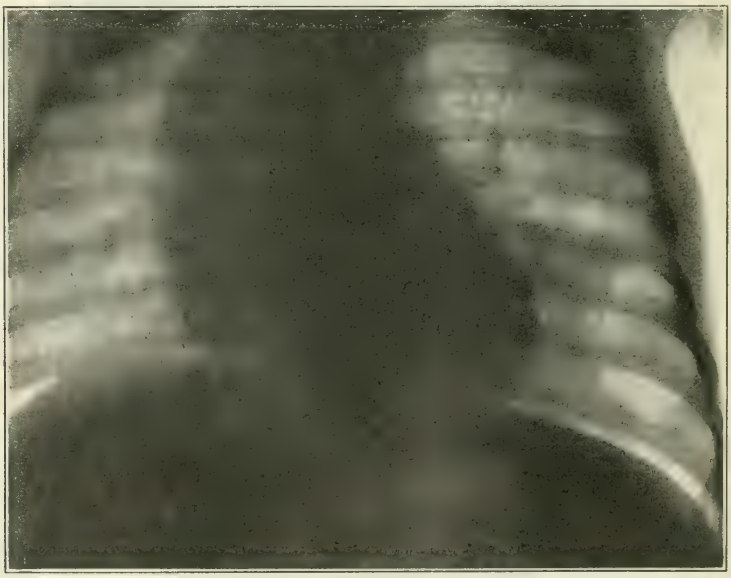

FIG. 4.—A perihilus, bronchopneumonic process of the left lower lobe; likewise a diffuse and unilateral enlargement on the right side, suggesting a universal involvement of all glands on this side.

lunged, the process merges into the secondary bronchopneumonic type.

2. The bronchopneumonic or lobular type may be a bronchopneumonia from the very beginning, or it may be, as described

FIG. 5.—An example of latent tuberculosis with right-sided paratracheal gland

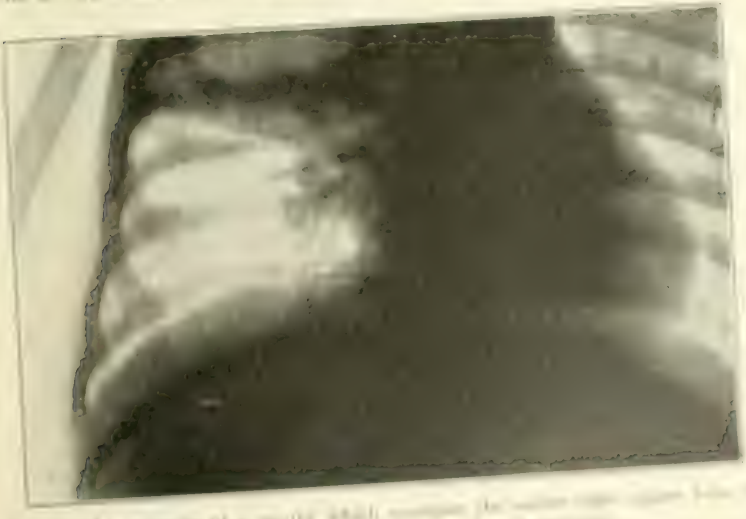

FIG. 6.—An example of a rapidly spreading [illegible] with [illegible]

above, a stage in the bronchitis type. The lobular type may be an isolated area of involvement in any of the lobes, more often the lower, and usually peribilar in site, or there may be a general diffuse extensive involvement, no area larger than 1 cm. in diameter

In the first instance the parenchymal process may retrogress, the glandular condition partially subside and a period of latency varying in time may intervene, followed by a flare-up of pathology. This may be repeated and go into a characteristic tuberculous process or subside completely without any parenchymal scars. The glands, however, always bear traces. This is the recurrent perihilus, pneumonic type, the differentiation of which is so difficult and the exact diagnosis so often overlooked.

In the cases of diffuse involvement the whole lung is so riddled that few areas of normal tissue are distinguishable. Complicating this picture, are minute effusions, fine fibrous bands, and occasionally localized areas of thickened pleura. A plate of this type shows every conceivable pulmonary change; small cavities, glands, large areas of amalgamated pathology, and occasionally small areas of spontaneous pneumothorax due to ruptured pulmonary tissue.

3. The lobar type or massive tuberculosis is probably the rarest of all types. We have had instances of not only involvement of one entire lobe right from the beginning, but we have seen an entire lung disabled, so that it was impossible to eliminate the diagnosis of effusion, so similar was the plate pathology. Only repeated negative aspirations and autopsy findings overcame our hesitant interpretation. The course of this type of pneumonia was in two directions.

In one type, a retraction of pathology to a small area and a definition of the process to only part of the lung takes place. This is an instance of the massive response of the organism where the actual area of involvement was considerably less than the early changes depicted. The process now assumed a characteristic and definite evolution to a central area of softening and a typical abscess cavity. Practically no fibrous walling off takes place, and if the condition is permitted to continue its way, the abscess breaks through and we see a localized pneumothorax. Abscess cavities may be single or multilocular, minute or the size of the better part of an entire lobe. If, however, as in the second type, the infection is overwhelming and death intervenes early in the disease, the process may end with a lobar involvement without abscess formation. This shadow is almost liver-like in its quality.

In all types the other lung may remain comparatively free without any determinable changes for a considerable time after the original process has been seen, but inevitably involvement of one type or other takes place. The guiding post in diagnosis in the early stages is the usual concomitant glandular involvement. Prognosis, of course, is bad.

Annular Shadow. We mention this because we have had two instances of this present in infancy; in one case with a bronchopneumonia and glandular changes suggestive of tuberculosis, and in the other, without any tuberculous pathology. There are no

tuberculous stigmata, and at the last observation, it is still present. Inasmuch as the significance of this is *subjudice*, we present this evidence for what it may be worth.

We take without question the use of the roentgen-ray as an adjuvant to exact diagnosis of tuberculosis in the later years of life. Why not broaden its application to infancy and the preschool age? Modern medicine, with its emphasis upon *prevention* should avail itself of this assistance. Surely, there are no technical difficulties, as any patient roentgenologist can prove. If the interpretation is still groping, then only wider experience can overcome that lack.

For prognosis its value is incalculable. For assistance in exact diagnosis in infancy when clinical signs are confusing, we cannot overestimate its value, not only in tuberculosis but in respiratory infections of all kinds.

Conclusion. Tuberculosis in infancy is of two types, acute and chronic; the first is the more common of the two and may be subdivided into:

1. Tuberculosis of the glands.
2. Tuberculosis of the lungs.

In both cases, by means of roentgen-ray follow-up, the process can be shown to have a definite and fairly orderly sequence, a period of congestion, a period of retraction or spreading, complete or incomplete and a period of softening.

While it is true, in the early or congestive stage, the process may not be distinguishable from any of the acute infections, in the second stage, of retraction or expansion, the condition assumes characteristic appearances and in the third stage, of pathology, there should be no difficulty in diagnosis.

For exact visualization of these changes, repeated and roentgenographic investigation is absolutely essential.